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THE CLINICAL SIGNIFICANCE OF AURICULAR FIBRILLATION

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ST. LOUIS
AND
E. O. JEFFREYS, M.D.
CHICAGO

Some thirty years ago Mackenzie observed that in certain cases of auricular fibrillation a conspicuous reduction of ventricular rate follows the administration of digitalis. Mackenzie believed that the accompanying relief of symptoms probably was to be attributed to the slowing, a conception elaborated and strengthened by Sir Thomas Lewis. Knowing of no beneficial effect of digitalis on the musculature of the failing ventricle, Lewis referred clinical improvement entirely to reduction in rate. The slowing was explained as due to a measure of auriculoventricular block induced by a special action of the drug on the connecting tissues. Since block of moderate extent will slow the ventricle only in cases of auricular fibrillation, this explanation logically limited the use of digitalis to cases of that arrhythmia. Lewis has held, furthermore, that the existence of established fibrillation implies disease of ventricular muscle and that the congestive heart failure which is present in most cases results from the tachycardia of the abnormal rhythm. On these postulates it has regularly been taught that digitalis should be employed to control ventricular rate in auricular fibrillation; if heart failure is present the ventricle will be relieved of the harmful effect of tachycardia and allowed to recuperate; if heart failure has not yet appeared, the block-producing action of the drug will protect the ventricle from rapid beating and thus tend to prevent failure; in all cases the drug should be used.

Under this conception, the significance of auricular fibrillation in any case is quite simple. It embodies merely the obligation properly to administer digitalis. At present, however, many physicians, while adhering to this time honored conception in its essential aspects, still entertain certain notions which in one or another particular are quite at variance with the premises on which it was founded. Interest is being manifested in the question of the cause of the abnormal rhythm as well as in the problem of management. More than once, in recent years, attention has been called to the existence of established fibrillation with neither heart failure nor heart disease. By almost every one it is now agreed that the use of digitalis should not be limited to cases of auricular fibrillation but that regularly in congestive heart failure the drug is of great value because of an effect directly on the muscle of the ventricle—an effect independent of rate or rhythm. Increasing attention, moreover, is being given to the observation made by Mackenzie that, in certain cases of the arrhythmia, digitalis causes no slowing in rate. There is an increasing tendency to omit the drug in special cases.

We have come to think of auricular fibrillation as follows: In certain situations some unusual factor may act on the wall of the auricle in such a way as to initiate the abnormal movement. It is to the underlying disorder rather than to its manifestation that chief attention must be given in diagnosis and in therapy; digitalis may or may not be indicated. This point of view is not new but it appears not yet to be very generally held. It has been our impression that in fibrillation it is only in cases of congestive heart failure that therapeutic doses of digitalis produce ventricular slowing and that in other cases no occasion exists for employment of the drug.

OBJECT AND PLAN OF STUDY

In order to check the correctness of this notion, we made a detailed study of the records of the Barnes Hospital. An additional object was to note the clinical conditions associated with the abnormal rhythm, data which might throw light on the problem of etiology.

Beginning with July 1, 1925, 431 consecutive case records of fibrillation were investigated. We recorded the sex, the age, the principal diagnosis, the cardiac diagnosis, the electrocardiographic diagnosis (in addition to that of auricular fibrillation), the presence or absence of any evidence of heart disease, the etiologic type, evidences of specific valvular lesions, the changes found at autopsy with regard to the auricle, the presence or absence of toxic agents and of fever, whether or not the auricular fibrillation stopped, whether or not there was any evidence of heart failure, whether or not digitalis was employed, the amount and period of time of administration, the change in heart (or pulse) rate after digitalis, other cardiac therapy, surgical operations and the hospital "result."

RESULTS

Heart Disease.—In 253 of the cases the principal diagnosis was related to the heart; in 178 cases it was noncardiac. Electrocardiograms were made in 387 cases. In 256 the record was thought to indicate some abnormality other than the arrhythmia, in 131 no other abnormality. Including secondary diagnosis, mention was made of some cardiac abnormality in addition to auricular fibrillation in 375 cases. In the remaining fifty-six cases no cardiac diagnosis was recorded, but study of these records showed that in fourteen some cardiac disorder might possibly have been suspected. Excluding these cases of "possible heart disease" there were left forty-two cases in which there existed no suspicion of anything wrong with the heart other than the auricular fibrillation itself. Examples of such cases are splenic anemia, fracture of the skull, carcinoma of

From the Department of Medicine, Washington University School of Medicine, and the Barnes Hospital, St. Louis.

the uterus, carcinoma of the mouth, carcinoma of the cervix, ureteral colic, strangulated hernia, embolism of the pulmonary artery, and neuralgia of the fifth cranial nerve.

Type of Heart Disease.—There were the following diagnoses of heart disease: rheumatic, 136; "arteriosclerotic," 114; hypertensive, 55; thyroid, 57; syphilitic, 7; miscellaneous, 6; no cardiac diagnosis, 56. As just stated, this group of fifty-six cases presenting "no heart disease" was further reduced to forty-two by exclusion of certain cases in which it appeared possible that minor degrees of heart disease might have escaped attention.

Valvular Lesions.—In many instances, diagnosis of more than one valve lesion was recorded. The following enumeration was made: mitral stenosis, 119; mitral insufficiency, 127; aortic stenosis, 21; aortic insufficiency, 30; tricuspid stenosis (autopsy confirmation), 1; tricuspid insufficiency, 6. The total number of cases presenting a valve lesion amounted to 230, and the total number of cases without evidence of valve lesion was 201.

Heart Failure.—All cases with a recorded diagnosis of heart failure were segregated. To this group were added all records which gave any evidence that some degree of heart failure might possibly have existed. There were 334 cases in this "heart failure" group, leaving ninety-seven cases in the non-heart failure group. Division was made on this basis with the particular object of studying the effect of digitalis in the absence of congestive heart failure, care being taken to exclude questionable cases. It is possible, therefore, that the actual number of cases of failure may have been somewhat less than 334.

Sex and Age.—There were 220 males and 211 females in the series. Ten patients were under 20 years of age, seventy under 40, and 150 under 50; 281 patients were 50 years of age or more and 167 were 60 or more. Fifty-five patients were as old as 70.

Autopsy.—Autopsy records were included in sixty-eight case histories. Most of them unfortunately followed the usual rule of centering attention on the ventricle, but in eighteen cases it is noteworthy that data were recorded relating to the auricle. The predominant changes were scarring, fibrosis, mural thrombi (some organized) and dilatation.

Toxemia and Fever.—In 280 cases there was evidence of toxemia or fever, or both.

Nervous Factors.—In a certain number of cases the chief if not the sole factor in the cause of the abnormal rhythm appeared to be of reflex nervous origin. Examples are neuralgia of the fifth cranial nerve, ureteral colic, thrombosis of the lenticular striate artery, and fracture of the skull.

Cessation of Auricular Fibrillation.—There were fifty-four cases in which the arrhythmia ceased either temporarily or for the remainder of the patient's hospital residence, in some of which it had begun after admission. Thirty-three were in patients with heart disease, twenty-one in the group without heart disease. These temporary cases were divided roughly into the following subgroups: (*a*) Recurrent or intermittent cases with so-called spontaneous cessation in which the exact causes of the cessation of the arrhythmia could not be determined. (*b*) Cessation with quinidine. This group cannot be divided sharply from the preceding group. (*c*) Cases in which the arrhythmia occurred with a known excitant and ceased with subsidence of its effect. Examples are onset after administration of vaccine, insulin or digitalis; with an anesthetic, and after operation. In this group should be included those cases of thyrotoxicosis in which the fibrillation stopped after thyroidectomy and perhaps such cases as pneumonia and other intoxications with temporary auricular fibrillation. (*d*) A few cases of heart failure of moderate degree in which the abnormal rhythm stopped after improvement with digitalis.

Surgical Operations.—Operation was performed in forty-eight cases in which auricular fibrillation was present before and at the time of operation. There were two deaths, both after operation. In neither case was there evidence that the auricular disorder was in any way responsible for the fatal outcome, one patient dying of hemorrhage and the other of pneumonia.

Digitalis.—Digitalis was administered in 341 cases and was not given in ninety. Taken as a whole, the series, covering a period of about ten years, gives evidence of no consistent policy for determining whether or not to administer the drug in cases of auricular fibrillation. It does show, however, that the proportion of all cases in which digitalis was given was higher in the earlier years, while as time went by there was an increase in the proportion of cases in which the drug was withheld. This applies particularly to cases in which there was no evidence of congestive heart failure. This tendency to give digitalis less regularly in cases of the arrhythmia without heart failure shows that among the staff members auricular fibrillation per se came less and less to be regarded as a specific indication for digitalis but that in cases of auricular fibrillation digitalis administration came more and more to depend on the general indication of congestive heart failure. In certain cases in spite of heart failure digitalis was regarded as contraindicated. In some there had been overdigitalization, in others thyrotoxicosis or other toxemia or some such attendant circumstance as coronary thrombosis was given as the reason for withholding the drug. In still other cases with a recorded diagnosis of heart failure no reason for withholding the drug was given, the physician apparently not having been impressed with any data which might have caused the diagnosis of failure to be entered on the record. All in all, of the ninety instances of auricular fibrillation in which digitalis was not administered, forty were cases of heart failure (or possible heart failure) and fifty were in the non-heart failure group (no suspicion of heart failure).

With the administration of digitalis in cases of heart failure, whether accompanied by auricular fibrillation or not, this study is not concerned. There is general agreement that, except for unusual circumstances, patients with congestive failure accompanied by auricular fibrillation should receive the drug. Authorities almost without exception now agree that other patients with heart failure also should get it. With regard to the indication for digitalis in cases of auricular fibrillation without congestive failure, however, disagreement in opinion if not in practice still exists. It was to the effects of the drug in such cases in this series that our attention was particularly directed.

Effects of Digitalis in Non-Heart Failure Cases.—Of the ninety-seven cases without suspicion of congestive heart failure, digitalis was administered in forty-seven and not given in fifty.

In the no-digitalis group were twelve cases of thyroid disease, four of carcinoma, two of cataract, two of hernia, and one each of enlargement of the prostate,

fracture of the skull, diabetes, urticaria, acute yellow atrophy of the liver, neuralgia of the fifth nerve, after vaccine administration, cholecystitis and pulmonary embolism. Twelve cases were listed as "not treated," twenty-eight as "improved," six as "not improved." There were four deaths.

In the digitalis group were seven cases of pneumonia, seven of thyroid disease, four of carcinoma, two of cholecystitis, two of enlargement of the prostate, one each of tabes, mesenteric thrombosis, after insulin administration, cataract, strangulated hernia, fracture of the femur, and tuberculosis of the vertebra. The hospital results showed twenty-eight as "improved," six as "not improved." There were thirteen deaths.

Although the mortality was higher in the digitalis group, it might be argued that this group contained a larger number of extremely ill patients, a postulate difficult of refutation or of substantiation. In at least one instance of intravenous administration death was attributed by the physician to digitalis. In most of the other cases there was little direct evidence that the drug did harm, but neither was there any evidence of any beneficial effect. In none of these cases without heart failure did the record give evidence of any slowing effect on the ventricular rate. In three of the fatal cases there was an acceleration after digitalis. In one (carcinoma of the cecum), 18 cc. of the tincture was administered the day before death; in another (strangulated hernia), 12 cc. of an intravenous preparation administered in twelve hours was followed by 0.1 Gm. daily; in the third (postoperative pneumonia), 1.2 Gm. was given in twelve hours.

INTERPRETATION OF RESULTS

Whatever the ultimate factors, it is obvious that the immediate causes of the abnormal auricular movement must be applied to the wall of the auricle, acting on the muscle or nerves (or both). It appears that in most cases heart disease is an important factor, whether its effects are directly or indirectly applied to the auricular wall. That organic heart disease is not necessary to the occurrence of fibrillation is indicated by the fact that it was not present in about 10 per cent of the cases. This occurrence of auricular fibrillation in patients without heart disease is in accord with the recent studies of Fowler and Baldridge,[1] Friedlander and Levine,[2] Orgain and White,[3] and others. While in most cases some pathologic process of the auricular muscle doubtless is an important factor, minor lesions appear to suffice in many instances, and in others nervous factors alone. It has been explained as "the result of a 'trigger phenomenon' of neurogenic origin in many cases." [2] In one of our cases of recurrent fibrillation the patient stated that emotional excitement frequently caused a paroxysm. This is in accord with the long recognized influence of nervous effects as well as direct muscular factors on the production of the circulating wave in the auricle of experimental animals. Certainly the auricular arrhythmia per se can no longer be regarded as implying disease of the ventricle.

Analysis of these cases strongly suggests that, while reflex nervous influences and toxic agents often may be causative factors, the chief agent in the initiation of the abnormal rhythm in most instances is increase in intra-auricular pressure. The well recognized association of the arrhythmia with mitral valve disease and with congestive heart failure is conspicuous in this series. In explaining the association of fibrillation with mitral stenosis, the valve lesion usually has been regarded as in some way a contributory cause of the arrhythmia, while in explaining the common association of the disorder with congestive heart failure it has been assumed that the arrhythmia is the cause of the failure. Not only does this explanation of heart failure ignore the presence in these cases of such common etiologic factors as infection, strain and diminished blood supply —factors now regarded as prominent causes of failure —but it involves further fallacy. The mere association of two observed phenomena can give no implication of cause and effect in one direction more than in the other, unless supported by collateral evidence. The accumulated evidence indicates that congestive failure as well as mitral disease promotes the initiation of auricular fibrillation. Both tend to increase intra-auricular pressure. Such increase in pressure is known to cause auricular fibrillation in heart-lung preparations [4] and has long been implicated in the clinical [5] explanation of the disordered rhythm.

In this conspicuous association of auricular fibrillation with congestive heart failure we are aware of the impossibility of differentiating cause from effect, a difficulty which appears sometimes not to have been appreciated. In patients who first come under observation with congestive heart failure and auricular fibrillation, it usually is impossible to determine which of the two phenomena was first to occur; but on the basis of experimental and clinical evidence it would appear far more logical to explain the arrhythmia as resulting in part from the increase in intra-auricular pressure attendant on congestive failure than to explain the failure as a result of the abnormal auricular movement. In many patients who have been observed over a period of years, failure is known to antedate the onset of auricular fibrillation. It appears to be the precipitating factor in the initiation of the arrthythmia. In many patients with few evidences of congestive failure it may be the arrhythmia which first attracts attention. In some such instances of early failure the onset of auricular fibrillation may indeed have been a blessing in that it has pointed the way to proper, even if misdirected, therapy. In a recent study of great merit Nahum and Hoff [6] call attention to stretching of the auricle from the pressure of congestive failure as a precipitating cause of auricular fibrillation. They say: "It thus becomes clear why this irregularity is so often associated with heart failure, being rightly regarded as an important evidence of the existence of heart failure." Stoppage of the abnormal rhythm after digitalis in a few of our cases with moderate heart failure suggests that the crucial factor in the restoration of normal rhythm may have been a decrease in intra-auricular pressure consequent on improvement in the circulation from the drug.

Stretching of the auricle alone, however, whether from ventricular failure or from mitral stenosis, usually does not suffice to cause clinical auricular fibril-

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2. Friedlander, R. D., and Levine, S. A.: Auricular Fibrillation and Flutter Without Evidence of Organic Heart Disease, New England J. Med. **211**: 624 (Oct. 4) 1934.

3. Orgain, E. S.; Wolff, Louis, and White, P. D.: Uncomplicated Auricular Fibrillation and Auricular Flutter: Frequent Occurrence and Good Prognosis in Patients Without Other Evidence of Cardiac Disease, Arch. Int. Med. **57**: 493 (March) 1936.

4. Kountz, W. B.: Personal communication to the authors.

5. Vaquez, Henri: Diseases of the Heart, Philadelphia, W. B. Saunders Company, 1924.

6. Nahum, L. H., and Hoff, H. E.: Auricular Fibrillation in Hyperthyroid Patients Produced by Acetyl-β-Methylcholine Chloride, with Observations on the Rôle of the Vagus and Some Exciting Agents in the Genesis of Auricular Fibrillation, J. A. M. A. **105**: 254 (July 27) 1935.

lation. As a rule it is effective only in cases in which it appears that certain changes have occurred in the auricular wall. The relative rarity of the arrhythmia in children is well recognized even though in them rheumatic heart disease predominates. In our series the association of auricular fibrillation with older age indicates that changes such as are incident to advancing years constitute an important contributory factor. The autopsy reports give the same implication. In view of the great effect of digitalis on ventricular rate in heart failure cases of auricular fibrillation, the failure of the drug to produce slowing in the non-heart failure cases is highly significant. It appears that slowing is related to its beneficial action on the muscle [7] in heart failure—an action whereby the heightened irritability of the musculature is reduced.[8] But it is only on the failing ventricle that digitalis lessens excitability. In toxic cases without failure it may even make the muscle more irritable.

SUMMARY

Auricular fibrillation may result from various influences acting on the muscle or nerves of the auricle. In some cases muscular effects are chiefly if not wholly responsible; in others nervous factors, direct or reflex, constitute the sole or predominating influence. Ultimate causes include toxemia; various nerve reflexes, central, abdominal, peripheral; nervous or emotional stress; lesions of the auricular musculature, and increased intra-auricular pressure. This study of 431 consecutive cases suggests that the commonest determining factor is increase in intra-auricular pressure from congestive heart failure or from mitral disease, exerted on the wall of an auricle which is the seat of changes such as occur with older age. Congestive heart failure is the commonest cause of auricular fibrillation.

Auricular fibrillation calls for examination. Search should be made for other evidences of toxic or nervous disorder and for other signs of heart failure. In a certain number of older patients the abnormal rhythm may be the first sign of congestive failure to attract attention, and in such instances obviously digitalis is indicated, as in other cases of heart failure. If exact etiologic diagnosis is obscure it may become appropriate to administer digitalis as a therapeutic test, but such experimental administration should no more be confused with specific therapy than should the administration of quinine in cases of unexplained fever. Seldom if ever is auricular fibrillation per se an indication for digitalis.

In non-heart failure cases of the arrhythmia, the administration of therapeutic doses of digitalis produces no slowing of ventricular rate. In a few such cases in this series, digitalis intoxication of greater or less degree was induced, a danger which appears not to be inconsequential if the drug is used in any attempt to slow the rate in toxic cases.

Auricular fibrillation is a result, not a cause, of some disorder that may need treatment. In cases of congestive heart failure with fibrillation the heart failure should be treated as in other cases of failure—with digitalis. In toxic or nervous disorders with the arrhythmia, treatment likewise should be the same as in similar cases with normal rhythm, thyroid disease should receive appropriate therapy, toxemia should be combated, nervous factors allayed. In both classes of cases (with and without heart failure), auricular fibrillation is a sign in diagnosis, not a disease per se. Occasionally the cause of the arrhythmia cannot be found or controlled, and the symptoms may be so prominent as to call for special therapy. In many such instances the disorder may be obliterated with quinidine.

It is no more correct to administer digitalis regularly on all occasions of fibrillation than it is to perform thyroidectomy, although each procedure is helpful in appropriate cases. A standard pattern of treatment is no more applicable in auricular fibrillation than in enlargement of the liver, in chills, in simple tachycardia or in edema. It is not to the sign but to the disease which produces it that treatment must be directed.

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IMMUNITY AND PROPHYLAXIS IN POLIOMYELITIS

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It is generally known that poliomyelitis virus possesses a high degree of host specificity, man alone being susceptible to natural infection. With the exception of certain Old World species of monkeys, lower animals of all kinds are refractory to it. Even those species of monkeys which yield to experimental inoculation never contract the disease spontaneously from infected associates. They also are therefore endowed with a fair degree of natural resistance, differing from the natural state in man in that quite artificial conditions must be imposed to induce infection. This difference in susceptibility, incidentally, must be borne in mind in the application of experimental results to man.

The resistance exhibited by naturally refractory animals does not appear to be related to humoral antibodies, for the serum from such animals rarely inactivates the virus in vitro even when a high ratio of serum to virus is employed. On the contrary, it appears to rest largely or wholly on tissue resistance, possibly simply on an indifference on the part of the nerve cells to the presence of the virus.

In those animals which yield to experimental inoculation, marked individual differences in resistance may be recognized. This individuality may be elicited by the use of graded doses of virus and by noting differences in the extent of the paralysis in animals inoculated with the same dose of virus. Epidemiologic and clinical observations suggest that marked individual differences in native resistance exist in man also. There is indeed some justification for believing that an important factor in determining the outcome of an exposure to infection in man is the general level of tissue resistance with which the individual has been naturally endowed, frank paralytic poliomyelitis probably being restricted largely to those members of society whose nerve cells, genetically speaking, are constitutionally inferior so far as resistance to this particular virus is concerned. This is in a measure reflected by the fact that approximately three fourths of normal young adults in urban communities exhibit indirect evidence of naturally acquired active immunity, though it must be admitted that a demonstration of neutralizing properties in the serum of persons not giving a history of the disease does not necessarily mean that these individuals have really acquired actual immunity to the disease as the result of contact with virus. The exceedingly variable clinical course in those who do develop frank poliomyelitis may

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be regarded as further evidence of individual differences in susceptibility to this disease, the more vulnerable individuals apparently being the exception rather than the rule.

While it is a well established fact that naturally acquired active immunity to this disease is commonly associated with humoral antibodies, it is not evident that these play a significant rôle in determining recovery or that they figure largely in the refractory state which follows recovery. Recent investigations have in fact shown quite conclusively that immune serum, even when administered to monkeys in very large doses, does not afford significant protection against virus inoculated by the intranasal route. This failure of the humoral factor to rally to the defense of the body may be explained by the fact that the virus normally gains admission to the central nervous system by the olfactory nerves, the terminals of which lie free on the nasal mucosa and therefore probably are largely or entirely unguarded by humoral antibodies. Once the virus has become established within this portal, it continues to be largely out of the reach of humoral antibodies. This is evidenced by the fact that a very large dose of highly active immune serum administered as early as two days after intranasal inoculation does not in any way alter the course of an experimental infection. It is now known that the virus is a strict neurotrope which travels from one level of the nervous system to another largely or entirely by axonal paths, probably inside neurons and therefore essentially out of the reach of circulating antibodies. Such limited protection as immune serum may afford against subsequent experimental inoculation by the intranasal route (in my experience less than 25 per cent) may be accounted for in part by the fact that the technic of infecting monkeys by this route may result in a local inflammatory response, with possibly sufficient exudation of the immune serum injected to inactivate virus adhering to the mucous surface and furthermore by the fact that monkeys are, in comparison with man, fairly resistant to infection by this route. Since inflammatory exudation is normally not apt to aid man at the time of exposure and since he is more susceptible to natural infection than monkeys, it would appear that humoral antibodies must play little or no rôle in human resistance to this disease.

What significance then is attached to the humoral antibodies which are so commonly associated with naturally acquired active immunity? While the answer is still not entirely clear, there are rather definite indications that they represent merely an adventitious by-product of infection; a general response to virus which has escaped from infected neurons, whether these have been damaged or not, and that the real basis of the immunity which follows infection is not humoral in nature but rests very largely or entirely on a cytoplasmic modification of previously susceptible neurons. In other words, the humoral antibodies are to be looked on as a reflection of the fact that the nerve cells have actually been exposed to the modifying influence of virus, for the modification, whatever its exact nature may be, seems to depend on intimate contact of the neurons with the causal agent. This cytoplasmic modification may not be at all associated with the formation of antisubstances but consists rather of the acquirement of new properties which leave the cells indifferent to the presence of this virus—traces of which may indeed persist for a time in the tissues, as seems to be true in certain other virus diseases.

A clear recognition of these relationships is obviously necessary for an understanding of the problem of creating resistance by artificial means. It is now known that passive immunization is not very effective against infection by the natural route; also that, while some increase in resistance may be brought about by the repeated injection of large doses of active virus over a sufficiently long period, the response to such injections seems to be largely, if not entirely, humoral in nature and is not associated with a significant increase in tissue resistance. What is of great practical importance is that, when the virus has been inactivated by physical or chemical means to make it safe as a vaccine, even the humoral response tends to drop out of the picture.

In the light of these facts the practical problem of creating resistance by artificial means assumes discouraging dimensions. Enough is now known about the pathogenesis and basis of immunity in this disease to justify considerable doubt that its control will ever be solved by means of serums or vaccines. It seems clear that a solution must be sought in new directions and the possibility that a practical solution may lie in a less orthodox direction does not seem entirely out of consideration. Indeed, a new hope has emerged from recent observations by Armstrong and Harrison,[1] Olitsky and his associates[2] and Gebhardt and myself,[3] which indicate that certain essentially harmless chemical agents once thoroughly applied to the olfactory mucosa of monkeys may afford protection against the virus for several weeks to several months thereafter. The substances which fall into this category are varied in composition and include alum, tannic acid, trinitrophenol (picric acid), zinc sulfate[4] and certain dyestuffs. Their modes of action may differ, but the protective effect is nevertheless exhibited in varying degrees by a number of these agents. It is already known that certain ones, once thoroughly applied, may provide protection for as long as three months. Since the protection may last for some weeks, it appears that the effect which they produce is not due to a virucidal action but depends on some modification in permeability of the normal portal of entry. Though by no means fleeting, the effect is temporary, since most animals do succumb in time to repeated intranasal instillation of virus.

From the general facts brought into this review, it seems clear that the trend of future investigations, so far as they relate to personal prophylaxis, should and very likely will center around means of guarding the olfactory area against the establishment of the virus at this point. Since certain chemical agents have already been found to exercise protective action in monkeys, further investigations along this line are clearly indicated. More work needs to be done in an effort to elicit the most satisfactory agent for human application, to determine precisely how the various chemoprophylactic agents act, and to determine the duration of the

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2. Sabin, A. B.; Olitsky, P. K., and Cox, H. R.: Protective Action of Certain Chemicals Against Infection of Monkeys with Nasally Instilled Poliomyelitis Virus, J. Bact. **31**: 35-36 (Jan.) 1936; J. Exper. Med. **63**: 877-892 (June) 1936.

3. Schultz, E. W., and Gebhardt, L. P.: Prevention of Intranasally Inoculated Poliomyelitis in Monkeys by Previous Intranasal Irrigation with Chemical Agents, Proc. Soc. Exper. Biol. & Med. **34**: 133-135 (March) 1936; Chemoprophylaxis of Poliomyelitis, California & West. Med. **45**: 138-140 (Aug.) 1936.

4. Observations since this paper was read in London indicate that zinc sulfate (from 0.5 to 1 per cent) is the most effective of the agents we have studied thus far; about 95 per cent of a total of fifty-three monkeys have resisted virus inoculated intranasally as long as a month after treatment of the nasal mucosa with this chemical, while about 95 per cent of an almost equal number of untreated controls developed the disease.

protection each affords, together with any harmful effects they may have on the tissues of the individual so protected, which would contraindicate their use. It must, of course, be borne in mind that results obtained in experimental animals are not always directly applicable to man.

While the use of chemical agents in this way may have application against diseases other than poliomyelitis, the possibility should be borne in mind that an agent which is effective in protecting against one virus disease may not necessarily be effective in protecting against another, even though the portal of entry may be the same. This much has already come out of comparative studies on poliomyelitis and St. Louis encephalitis, it being more difficult experimentally to protect against the latter than against the former disease.

That there may not be undue confusion later, it will be important for investigators to compare their observations with reference to a given disease, and certainly important to compare their results in terms of the procedures employed. There must, of course, be no uncertainty as to making good contact with the actual portal of entry, and such factors as the concentration of the agent, the nature of the menstruum, the temperature of the solution at the time of application, the number of applications and the interval between applications will all require careful attention and should be given in detail in publishing observations. It is to be hoped that, with the passage of time, chemoprophylaxis may come to be regarded as an effective aid in the control of this and possibly other virus diseases.

THE CLINICAL USE AND DANGERS OF HYPNOTICS

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The administration of hypnotics and of sedatives acting on the nervous system represents one of the most frequently used therapeutic procedures in medicine. Millions are spent for the purchase of these drugs and, as the result of popular interest, they are often used without medical supervision. Indeed, their consumption is so widespread that the question has been raised whether they may exert a deleterious effect on an appreciable proportion of the population.[1] In spite of the fact that these substances represent symptomatic remedies of great value, their use is not without danger. When they are administered intelligently, however, and with full knowledge of their pharmacologic and toxicologic properties, their beneficial effects distinctly outweigh the occasional untoward reactions. Instances are also not wanting in which the skilful application of these drugs has saved the patient's life.

There are few questions that recur in the minds of physicians as frequently as the following ones: When and how should hypnotics be used? What are their relative merits and contraindications? How long should their use be continued? How large a dose is it safe to administer? When should they be given by mouth and when parenterally? Will the patient develop a "habit" from their use? What is their effect on the heart and circulation? Is the sudden change in the condition of the patient following the administration of hypnotics due to the hypnotics or is it independent of them? Answers to these questions can be supplied only (1) through the appreciation of certain general established principles, (2) through specific knowledge bearing on the individual drug and (3) through full understanding of the patient as a psychophysical unit.

My purpose in this presentation is to discuss certain general principles bearing on the use of hypnotics. No attempt is made to describe the pharmacologic and therapeutic properties of individual drugs, as this has been done elsewhere.[2]

RELATION OF HYPNOTICS TO SEDATIVES, ANALGESICS AND ANESTHETICS

Hypnotics are drugs that induce sleep. Sedatives and analgesics are chemical agents that are supposed to decrease the sensitivity of the central nervous system and diminish or abolish pain. Anesthetics, or narcotics, in the strict sense of the word, are substances that depress the central nervous system, abolishing certain types of sensations. Such a classification, however, is quite arbitrary and unsatisfactory from a clinical point of view because the same drug in varying dosage is used as an analgesic, a hypnotic or an anesthetic. Furthermore, if sleeplessness is caused by pain, an analgesic becomes a hypnotic, and, contrariwise, true hypnotics may act indirectly as anodynes. Finally, some hypnotics, such as tribrom-ethanol, are often used as anesthetics. Hence, sharp separation between these types of drugs, so far as effect is concerned, is not feasible. From a clinical point of view, all drugs that can be administered without unpleasant side action and that decrease the sensitivity of the central nervous system selectively or diffusely are sedatives in the broader sense. Within the group of sedatives there exist substances which in large doses induce sleep with regularity. These drugs are hypnotics.

TYPES OF SLEEP AND THE CHOICE OF HYPNOTICS

Hypnotics are symptomatic remedies, and they represent only one of the measures that are of aid in inducing sleep. Frequently, psychotherapeutic or physical measures directed at the core of the problem are to be preferred, and hypnotics serve but as adjuvants. An ideally correct selection of a soporific for a given patient will be possible only when both the mechanism of the disturbance of sleep and the manner of action of the drug to be used are known. Much will be accomplished through a better understanding of the interrelations between certain functions of the cortex, the diencephalon and the mesencephalon, on the one hand, and through the better localization of the seat of action of the sedatives and hypnotics, on the other hand.

All that is known today is that in the brain stem there exist areas the physical or chemical disturbance of which can result in an instantaneous sleeplike state.[3] The nervous centers responsible for regulation of con-

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1. Mörchen, F.: Die Schlafmittelfrage, Deutsche med. Wchnschr. **60**: 798 (May 25) 1934. Flury, F.: Schlafmittelmissbrauch, ibid. **60**: 1155 (Aug. 3) 1934.

2. Weiss, Soma: (*a*) The Therapeutic Indications and the Dangers of the Intravenous Administration of Sodium-Phenyl-Ethyl Barbiturate (Sodium Luminal) and Other Barbituric Acid Derivatives, Am. J. M. Sc. **178**: 390 (Sept.) 1929; (*b*) The Indications and Dangers of Sedatives and Hypnotics with Special Reference to the Barbituric Acid Derivatives, Internat. Clin. **1**: 39 (March) 1936.

3. Hess, W. R.: The Autonomic Nervous System: Sleep as a Regulating Process, Lancet **2**: 1259 (Dec. 10) 1932. Ferris, E. B., Jr.; Capps, R. B., and Weiss, Soma: Carotid Sinus Syncope and Its Bearing on the Mechanism of the Unconscious State and Convulsions, Medicine **14**: 377 (Dec.) 1935.

sciousness and sleep are in some respects of parasympathetic character. Although recently acquired knowledge indicates that the different types of hypnotics reach diffusely all portions of the central nervous system,[4] there is nevertheless evidence that certain portions of the brain possess a selective chemical and functional susceptibility to the action of hypnotics. Thus, in spite of the fact that the barbiturates are taken up by all parts of the brain as well as by tissues of other organs, the disturbances of several vegetative functions in barbiturate hypnosis and the antagonistic effects of ephedrine, benzedrine and picrotoxin suggest a special reactivity of centers in the brain stem to this group of drugs. In this somewhat restricted sense there is justification for the division of hypnotics into two groups: one having predominantly a cortical action, such as bromides, paraldehyde, chloral hydrate, bromural and carbromal, and one having a relatively greater effect on the brain stem, such as the barbiturates.[5]

In the clinical selection of suitable hypnotics, an examination of the nature of the sleep habit of the patient is essential. It should be appreciated that sleep requirement varies considerably in normal persons. The refreshing effect of sleep is influenced by the degree of preceding physical and mental exertion, and particularly by emotional conflicts. In addition to the duration and the depth of the sleep, the character of the dream states is an important factor. The depth of sleep, as indicated by the intensity of stimulus required for awakening, is usually two or three times greater during the first two hours than thereafter, when slowly and progressively it becomes superficial.

In examining the more common types of disturbance of sleep, one finds that in persons who are nervously fatigued the difficulty often lies in the disturbance of the onset. Once sleep is established, the normal rhythm will continue. In such patients, mild or more potent hypnotics with short duration of action, such as bromural, carbromal or the sodium salt of *n*-methyl-cyclohexenyl-methyl barbituric acid (evipal), will be effective, with the advantage of no after-effects. In patients whose sleep remains superficial with frequent awakenings, milder hypnotics with relatively long duration of action, such as chloral, chloral hydrate, barbital, dial and phenobarbital, are indicated. In neurasthenic individuals the rapport between physician and patient is often symbolically transferred to the medication; hence even milk or water, with proper suggestion, often is effective. There is, however, a definite physiologic mechanism that is active here. The psychic factor also frequently plays a part in the effect of potent hypnotics. If the cause of disturbed sleep is pain, analgesics such as salicylates, acetophenetidin or codeine, administered alone or in combination with hypnotics, give good results, whereas hypnotics alone are ineffective. If motor restlessness is responsible for insomnia, as in infectious disease, hypnotics with dominant motor depressant effect, such as bromides and the barbiturates, are helpful. If a change is made from one type of hypnotic to another, it should be remembered that a synergism exists in their depressant effect on the vital centers. Hence, a full dose of any hypnotic can be given only after the dose administered previously is adequately eliminated.

These considerations indicate that hypnotics often do not act directly on the "sleep centers" but rather act indirectly through elimination of the factors interfering with natural sleep. Such indirect induction of natural sleep is always to be preferred to the "forced" action of hypnotics on the nervous mechanism of sleep, as the latter type of sleep, notwithstanding its depth and duration, is not natural and often not refreshing.

CLASSIFICATION OF SEDATIVES AND HYPNOTICS

The sedatives and hypnotics are of heterogeneous chemical types. While among members of the same group a certain degree of relationship exists between the chemical structure and pharmacologic effects, no such relationship exists between the various types. Thus, some inorganic salts, just like some complex organic substances, are mild while others are powerful hypnotics; some have a short and others a long duration of action.

Much vogue and fashion exists in the use of sedatives and hypnotics. Today some of the older members of the group, such as acetphenetidin, acetanilid, aldehydes and carbamates, have fallen into undeserved disuse, whereas the more recently introduced drugs, such as the barbiturates, enjoy a popularity not always deserved. One may, with reservations, group the substances frequently used as sedatives and hypnotics, according to increasing therapeutic potency and toxicity, as follows: (1) the acetophenetidins, salicylates and anilids (primarily analgesics); inorganic salts, such as bromides, calcium (analgesic) and magnesium salts; (2) the alcohol and aldehyde groups, as represented mainly by ethyl alcohol, tribrom-ethanol, trichlorisopropyl alcohol, chlorbutanol (trichlortertiary butyl alcohol), on the one hand, and paraldehyde and chloral hydrate (trichloracetaldehydrate), on the other hand; (3) the sulfones, as represented by sulfonmethane and sulfonethylmethane; (4) the ureids, as represented by carbromal (bromdiethylacetylurea) and bromural (*a*-monobromisovalerylurea); (5) the barbituric acid derivatives, as represented by a large number of substances, such as amytal, barbital, dial, ipral, neonal, nostal, pentobarbital, phanodorn, phenobarbital and sandoptal; (6) the hydrocarbons, such as acetylene, ethylene, cyclopropane, chloroform and ethyl chloride (used as anesthetics only), and (7) finally the morphine group, as represented by morphine, dilaudid and codeine. Some of these substances are primarily analgesic and do not possess a direct hypnotic effect, but they are often used as hypnotics because of their analgesic effects.

Chemical Structure and Pharmacologic Action.—There are a large number of hypnotics used in medicine, and the number of their theoretical possibilities is unlimited. Within the barbituric acid group alone, more than thirty preparations are available. These barbiturates, often recognized only through their trade names, are closely related both in chemical structure and in pharmacologic action. By altering the character of the side chains of their chemical structure, the main differences induced are (1) in the therapeutic and toxic doses, (2) in the induction and recovery times and, finally, (3) in the duration of sleep or persistence of action. The fact that the therapeutic dose of one substance is smaller than that of another does not indicate that the hypnotic is a better or a safer one. It is rather the ratio between the hypnotic and the toxic or fatal dose that is one of the important measures of pharmacologic fitness.

In spite of the fact that a certain type of chemical alteration tends to produce a certain type of change in the pharmacologic action, exceptions are not uncom-

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5. Pick, E. P.: Die Grundlagen der Schlafmittel-Therapie, Fortschr. d. Therap. **6**: 161 (March 25) 1930.

mon. Hence, careful pharmacologic and therapeutic study of each member is essential. The following examples will serve to illustrate the changes in pharmacologic effects resulting from simple chemical alterations: While the methyl sulfones and methyl barbiturates are practically inert, the introduction of ethyl radicals creates a potent hypnotic effect. As far as the barbiturates are concerned, the longer the alkyl side chain, the greater in general are the hypnotic and toxic effects. Moreover, the saturation of the side chain has a significant effect on the behavior of the barbiturates in the body. The unsaturated members are inactivated by the liver and hence usually have a shorter duration of action, while the saturated barbiturates are eliminated more or less unaltered by the kidney and usually act over a longer period of time. Thus the intravenous administration of *n*-methyl-cyclohexenyl-methyl barbituric acid (evipal), containing a "heavy" side chain which readily disintegrates in the body, produces hypnosis measured in minutes, while a corresponding dose of diethylbarbituric acid (barbital) or phenylethyl barbituric acid (phenobarbital), substances which are not metabolized, can cause sleep of many hours' duration. Equally striking changes in biologic action can be induced by the introduction of or changes in halogen atoms. The difference in the effect of ethyl alcohol and of tribrom-ethanol is an outstanding example of such a change in chemical structure and pharmacologic effect.

ADMINISTRATION AND DOSAGE

Administration of hypnotics should be by mouth unless this is not feasible or is contraindicated. When oral administration is not possible, a soluble preparation may be given rectally by means of a starch enema. In patients with ulcerative lesions of the stomach or the duodenum, irritative hypnotics, such as chloral and chloral hydrate, should not be given by mouth. Some of the special indications for parenteral administration are delirium with threatening circulatory collapse especially if the patient resists oral or rectal administration, convulsive seizures from local anesthetics, grand mal seizures, tetanus with a tendency to marked spasms and convulsions, and severe cases of eclampsia. For parenteral use, paraldehyde and the barbituric acid derivatives are particularly suitable. As these drugs are irritant when given subcutaneously, they should be administered intramuscularly or intravenously. Intravenous injections should be given slowly, in the form of a relatively dilute solution.

Dosage is a relative amount of a drug essential for a desired therapeutic effect. Depending on the effect desired, some of the hypnotics are used in as widely varying a range as from 1 to 30. It holds true for all hypnotics that the more irritable the central nervous system, the greater is the dose required to induce sleep. Thus, in nervously fatigued persons, phenobarbital is used effectively in doses of 30 mg. (one-half grain) to enhance the natural tendency to sleep. In the presence of convulsions, on the other hand, doses of 1 Gm. (15 grains) or more are required to abolish the seizure and induce sleep. Any intense stimulus acting on the central nervous system can, within limits, counteract the effect of sedatives and hypnotics of all sorts. Contrariwise, if external and internal stimuli influencing the patient are reduced or eliminated, the effective dose will be smaller. It is for this reason that establishment of the general comfort of the patient through good nursing is always an effective adjuvant of drug sedation. The administration of large doses of sedatives is justified only in serious emergencies, as previously indicated, and is attended with potential dangers.[2] One such inherent danger is the fluctuation in the state of irritability of the central nervous system. Thus, in order to overcome a convulsive seizure a relatively large dose of a hypnotic is essential. Following the cessation of the fit, however, the irritable state of the nervous system decreases, and frequently depression follows. In the latter state, then, the therapeutic dose administered under the former conditions becomes toxic.

In selecting the time of oral administration of hypnotics, the induction period is a determining factor. Certain hypnotics with a short induction period, such as chloral hydrate, paraldehyde, bromural, amytal and pentobarbital, can be taken effectively from one-half to one hour before retiring; others with a longer induction period, such as barbital, dial, ipral, phenobarbital and sulfonmethane, should be administered from one to two hours before the effect is desired.

The frequency of repetition of the dose depends on clinical indications and on the duration of action of the drug, and also on the patient's condition. Thus, in the presence of pain or muscular spasm, such as exists in tetanus, large doses of hypnotics with long duration of action may be efficacious for but three hours, while the same amount consumed by a normal person can produce deep sleep of several days' duration. Effort should always be made to discontinue the medication as soon as feasible. In case of prolonged use, it is preferable to change to other drugs of the same group or to another type of drug. It is also advisable not to prescribe hypnotics for more than two or three weeks without medical supervision. Such a procedure safeguards against the use of drugs for suicidal purposes.

UNTOWARD EFFECTS

Susceptibility to hypnotics depends partly on innate, partly on acquired, characteristics of the patient. Persons with sensitive and unstable nervous systems are particularly susceptible to the action of these drugs. Patients with anemia usually require smaller doses to achieve a given effect. As the detoxification and elimination of hypnotics are usually accomplished by the liver and kidneys, disease of these organs is frequently associated with increased susceptibility. Thus, the unsaturated barbituric acid derivatives, which are detoxified by the liver, can show intensified and prolonged action in the presence of diseases of the liver. I have observed two instances of poisoning with *n*-methyl-cyclohexenyl-methyl barbituric acid (evipal) of six and eight hours' duration in patients with liver disease following a dose which in a normal person would have a hypnotic effect for about twenty minutes. Other hypnotics that are not detoxified in the liver but are eliminated by the kidneys, such as bromides, barbital and phenobarbital, induce prolonged action in the presence of impaired renal function. It should also be borne in mind that regardless of through which organs hypnotics are metabolized or eliminated, inactivation is always dependent on an efficient circulation. Hence, in the presence of circulatory failure or collapse, effective elimination becomes seriously impaired and the hypnotic will remain active longer. Such prolonged action will then, in turn, add to the disintegration of the circulation, finally resulting in a vicious circle. This explains why drugs with a relatively short duration of action, such as tribrom-ethanol, can, in the presence of "shock," cause sleep of several days' duration. This is also one

of the main reasons why nonvolatile anesthetics are potentially dangerous agents in surgical practice.

When such pathologic states exist, particular precautions must accompany the use of hypnotics. Their careless use in peripheral circulatory failure, as judged from personal observations, is frequently responsible for fatalities, while the danger from direct action of hypnotics on the heart, often feared by physicians, is a negligible factor. In small therapeutic doses, hypnotics do not exert a detectable harmful effect on the heart.

Habit Formation and Addiction.—The evaluation of this problem is difficult, mainly because of the confusion that exists in the definition of terms. If one defines addiction as a bodily state which results in demonstrable disturbances of certain vegetative functions, such as occur after the withdrawal of morphine in habituates, then the commonly used hypnotics do not lead to addiction. On the other hand, it is common to find that, after prolonged administration of the members of the alcohol, aldehyde, urea or barbituric acid groups, patients crave their further use, and nervous disturbances may appear when they are discontinued. In this sense habit formation after the prolonged use of hypnotics is common. How far such habit formation is specific to the drug and how far it bears on the innate state of the patient it is difficult to judge. The prolonged use of these drugs is most common in individuals with emotional and mental difficulties, the very types of patients in whom not only formation of habits by suggestion but also development of conditioned reflexes occur with ease. Some of these subjects can acquire a habit to pink colored water if proper psychic influence is attached to its use. It is certain that in the majority of such instances the habit formation is psychologic. Nevertheless, in view of the fact that the difficulty experienced by the patient is practically identical regardless of whether the source of the habit is psychologic or chemical, every precaution should be taken to prevent the development of habit formation.

Idiosyncrasy.—Certain aspects of this problem bearing on susceptibility have already been discussed. Untoward reactions associated with confusion, lassitude, headache and accentuation of existing emotional states may occur after relatively large doses of any hypnotic, particularly in nervously hypersensitive persons. I have on several occasions observed that such drugs temporarily accentuated manic-depressive or paranoiac tendencies in subjects with mild psychopathic personalities. In some of these patients the transient psychotic state seen after relatively large doses of hypnotics becomes established years later. Similarly, it is not rare in hospital practice to observe that confusion and psychotic tendencies become accentuated in patients with cardiac decompensation or infectious or certain deficiency diseases following attempted sedation with paraldehydes, chloral hydrate or the barbiturates.

Sometimes, then, under the effect of hypnotics, the underlying and heretofore partially controlled mental aberration becomes aggravated or brought to the surface from a subclinical stage. Such untoward effects precipitated by hypnotics are often not recognized, and the condition is aggravated by the further increase or repetition of the drug. It is difficult to state whether one type of hypnotic has a greater tendency to precipitate such conditions than others. Delirium precipitated by morphine may subside when barbiturates are administered, and toxic psychosis accentuated by a barbiturate may disappear after the administration of paraldehyde. One cannot generalize, however, but usually under such circumstances it is advisable to discontinue drug therapy and apply physical measures.

I have observed, as have Castin and Gardien,[6] patients with psychoneurotic personalities and insomnia in whom barbituric acid derivatives apparently precipitated ill defined, severe pain in the muscles or joints. The pain may be intense, particularly in the early hours of the morning, and may last for days or weeks after the drug has been discontinued. It is localized most frequently over the neck, shoulder and scapular regions and in the arms, and may appear in paroxysms.

In recent years dilaudid (dihydromorphinone hydrochloride) has been widely used as a morphine substitute. This drug is frequently utilized under the misconception that it is safer than morphine and that addiction does not develop. The pharmacologic and chemical evidence thus far available, however, suggests that the ratio between effective and toxic doses of morphine and of dilaudid, respectively, is essentially the same.[7] While tolerance to dilaudid develops with somewhat less ease than tolerance to morphine, nevertheless addiction to this drug has been reported. Although dilaudid may offer some advantage over morphine under special indications, the optimistic expectation and careless use that followed its earlier clinical trial are not justified.

Idiosyncrasy in the form of allergic or allergic-like reactions also may develop. This is apt to occur in patients with a tendency to asthma, angioneurotic edema, urticaria and severe menstrual difficulties. The presence of liver or renal abnormality can accentuate such tendencies. Among these reactions are the skin lesions precipitated by the bromides; toxic hepatitis following the administration of chloral, chloral hydrate or paraldehyde, and swelling of the eyelids, cheeks and lips, erythema and other exudative skin lesions, and, rarely, exfoliative dermatitis following the use of relatively small amounts of phenobarbital, allyl-isopropylbarbituric acid with aminopyrine and other barbituric acid derivatives. Pronounced reduction of blood platelets with hemorrhagic manifestations may develop from sensitivity to allyl-isopropylacetylurea (sedormid). I have observed two instances of such purpura. Purpura associated with increased capillary permeability and without hemorrhage from mucosae and reduction of platelets apparently may rarely result from chloral and paraldehyde. Agranulocytic angina has been precipitated by aminopyrine, but evidence is lacking so far to indicate that any one of the barbiturates alone is responsible for the precipitation of this condition.

CHRONIC INTOXICATION FROM PROLONGED MEDICATION

If doses of hypnotics are repeated before complete inactivation or complete elimination has taken place, nervous manifestations will appear as a result of the slow accumulation. Some of the features of chronic intoxication are the same regardless of the hypnotic administered; for example, a gradual loss of ambition, impairment of capacity for concentration and increasing desire to sleep. With certain types of hypnotics, particularly of the barbituric series, bizarre disturbances of the nervous system can develop which, if not recognized, can offer puzzling diagnostic problems. Chronic

6. Castin, P., and Gardien, P.: Arthralgies et myalgies barbituriques, Presse méd. **42**: 1536 (Oct. 3) 1934.

7. Eddy, N. B.: Dilaudid (Dihydromorphinone Hydrochloride), J. A. M. A. **100**: 1032 (April 1) 1933. Dilaudid (Dihydromorphinone): A Review of the Literature and a Study of Its Addictive Properties, U. S. Public Health Rep. supp. 113, U. S. Gov. Printing Office, Washington, 1935.

barbiturate poisoning, which nowadays is by far the most frequently observed chronic intoxication due to hypnotics, may manifest itself in vertigo, ataxia, nystagmus, visual hallucinations, difficulties with visual accommodation, thick speech, difficulty in the use of or paralysis of the limbs, or tremor. Suppression of the normal reflexes and appearance of changes in the pyramidal tract can complicate the clinical picture. The manifestations at times closely simulate the picture of epidemic encephalitis, pseudobulbar palsy, acute psychic depression, delirium tremens and cerebral vascular thrombosis. The heart is not affected, but there may be a tendency to pulmonary congestion. Rarely, albumin and casts appear in the urine. These manifestations disappear after discontinuance of the drug, though it may take two weeks or longer for complete recovery. This rather long period, out of proportion to the time required for chemical elimination of the drug, suggests that chronic intoxication consists not only in lack of elimination of the drug but also in a toxic effect on the structure of the nerve cells. Experimental evidence supports such a contention.[8] The appearance of chronic intoxication does not necessarily indicate the complete abandonment of medication; it rather makes desirable the better regulation of the dosage or the change to a preparation that has a shorter duration of action.

ACUTE POISONING

Acute poisoning seldom occurs as a result of individual susceptibility or following the administration of large therapeutic doses of hypnotics. It more frequently is due to ingestion of massive doses taken by mistake or with suicidal intent. In order to avoid accidental poisoning, it is advisable to instruct patients and their relatives not to keep bottles containing hypnotics at the bedside. During sleep, or during the accentuated confusion and reduced inhibition following the taking of a therapeutic dose, patients may unintentionally or subconsciously take toxic amounts. The use of hypnotics, particularly the barbiturates, is becoming the vogue in suicidal attempts. In view of the fact that the efficacy of the treatment of poisoning from barbiturates and other hypnotics is increasing, and since no permanent disability follows these intoxications, such a change in the trend toward suicide with hypnotics is welcomed, because the prognosis is better than with similar attempts with other chemicals, such as mercury, phosphorus and saponated solution of cresol.

The differences in the behavior of patients intoxicated with various types of hypnotics are inadequate for the clinical diagnosis of the nature of poisoning. This should be determined through circumstantial and preferably through chemical evidence. The clinical course of intoxication is always potentially treacherous. The primary danger in acute intoxication is the derangement of vital nerve centers and, as a consequence, circulatory collapse. In addition, several of the hypnotics are capillary poisons and change their permeability. Some, such as chloral hydrate and paraldehyde, possess a relatively greater depressant action on the vasomotor system than others, like the barbiturates, and circulatory collapse can develop unexpectedly and with great rapidity. The full development of the intoxication may take some time, because nausea closes the pylorus and thus retards absorption. In addition, as has already been indicated, if there is a tendency to vasomotor collapse the inactivation of hypnotics becomes impaired and their action is prolonged and intensified. It is of practical significance that their depressant effect on the circulatory system is to some extent independent of their effect on the nervous system. Thus it is common experience to observe impairment of the peripheral circulation, pulmonary congestion and the development of a fatal bronchopneumonia days after the patient has regained consciousness. These late complications bear pertinently on the care of these patients.

The fatal dose of a hypnotic varies considerably, depending on factors already discussed. We[9] have shown elsewhere the synergistic and antagonistic relationship that exists between the state of the respiratory center and the action of respiratory stimulants on the one hand and the action of depressants on the other. As far as the barbiturates are concerned, it has been stated that even small average hypnotic doses can cause dangerous or fatal reactions in organically normal subjects. Gillespie[10] has recently examined the literature and concluded that there is no case on record in which either a single dose or repeated doses of average therapeutic magnitude have caused death in the absence of complicating factors. This obviously does not refer to the rare instances of fatal skin reactions.

Treatment.—In instances of mild intoxication, withdrawal of the hypnotic alone relieves the symptoms. The principles of treatment of severe intoxications are (1) removal of the hypnotic from the gastro-intestinal canal, (2) counteraction of the depressant action on the central nervous system, (3) prevention and treatment of circulatory collapse and its secondary complications, and (4) specific measures.

Gastric lavage should be performed with rather warm solutions, even if the patient is attended several hours after the ingestion of the drug, because absorption from the stomach may become slow with the onset of coma. Furthermore, a warm solution in the stomach is an effective general stimulant and supplies body heat, which is often disturbed under such conditions. The head should be kept low during and after lavage in order to prevent aspiration pneumonia, a not infrequent cause of death in an otherwise responsive type of case. Before the removal of the stomach tube, from 30 to 60 cc. (1 to 2 ounces) of a 50 per cent magnesium sulfate solution should be left in the stomach. With disturbed heat regulation, proper covering and heaters should be placed along the extremities. As a preventive of hypostatic congestion of the lungs and pneumonia, the body should be turned from one side to the other at approximately hourly intervals. An adequate amount of fluid should be administered, and for caloric supply intravenous dextrose solution may be given. If pulmonary congestion or vasomotor collapse exists, from 50 to 100 cc. (2 to 3 ounces) of 50 per cent dextrose solution should be infused intravenously.

The underlying principle of the drug therapy of poisoning with hypnotics is the administration of substances that increase the excitability of the central nervous system, particularly of those centers on which the hypnotics in question act predominantly. Caffeine, pyridine-betacarbonic acid, diethylamide (coramin) and

8. Pickworth, F. A.; Young, H. M. A., and Willcox, W. H.: Clinical and Pathological Effects of Hypnotic Drugs of Barbituric Acid and Sulphonal Groups, Proc. Roy. Soc. Med. (Sect. Therap. & Pharm.) **20**: 13 (July) 1927.

9. Norris, V. H., and Weiss, Soma: The Pharmacological and Therapeutic Properties of Alpha-Lobeline: A Comparison of Its Action on the Respiratory Center with That of Other Respiratory Stimulants, J. Pharmacol. & Exper. Therap. **31**: 43 (May) 1927.

10. Gillespie, R. D.: Discussion on the Uses and Dangers of the Hypnotic Drugs Other than Alkaloids, Proc. Roy. Soc. Med. **27**: 504 (Feb.) 1934; On the Alleged Dangers of the Barbiturates, Lancet **1**: 337 (Feb. 17) 1934.

strychnine are the drugs most frequently used. The effectiveness of these drugs has been demonstrated experimentally in such varying types of intoxication as those caused by morphine, chloral hydrate, tribromethanol and the barbiturates. Their dosage depends on the depth of the depression of the central nervous system. The improvement of the circulation following the administration of these substances is not due to direct action on the heart but rather to action on the vasomotor centers. Through the improved peripheral circulation, the detoxifying capacity of the body becomes increased; hence these drugs are more than symptomatic "awakening" remedies. The disadvantage of coramin is that the persistence of action is brief.[11] Haggard and Greenberg[12] have shown the efficacy of strychnine in experimental phenobarbital poisoning, and successful treatment of poisoning in man has been reported.[13] In severe types of poisoning I have administered strychnine at hourly intervals intravenously or subcutaneously, in doses up to 10 mg. (one-sixth grain). As improvement occurred the dosage was gradually decreased to 1 or 2 mg. ($\frac{1}{60}$ to $\frac{1}{30}$ grain). Ephedrine and related substances, such as benzedrine, can counteract sleep and stimulate centers in the brain stem. This action is beneficial in the treatment of experimental intoxication with hypnotics.[14] In severe barbituric poisoning I[2b] have administered from 15 to 30 mg. (one-fourth to one-half grain) of ephedrine intravenously or intramuscularly at two-hour intervals, alternating every hour with strychnine. Purves-Stewart and Willcox[15] have advocated in barbital poisoning repeated drainage of the spinal fluid through lumbar puncture, taps, or preferably through cisternal drainage. According to these observers this procedure hastens the removal of the drug from the central nervous system and especially from the vital medullary centers, which are bathed by the poison in relatively high concentration. I have used this procedure as an adjuvant in the treatment of poisoning with saturated barbiturates such as barbital and phenobarbital, which are not inactivated within the body and hence are present in relatively high concentration in the spinal fluid.

CONCLUSION

These are, then, some of the general aspects of the clinical problem of the hypnotics. For the skilful use of these substances, additional specific knowledge bearing particularly on the pharmacologic characteristics of individual hypnotics and on the clinical evaluation of the patient is essential. The effective use of hypnotics demonstrates the necessity of knowledge of clinical as well as of biologic sciences in the daily work of the physician.

In clinical practice, the use of a few well selected and well studied hypnotics included in the United States Pharmacopeia or accepted by the Council on Pharmacy and Chemistry of the American Medical Association will yield better therapeutic results than the use of a large number of poorly understood hypnotics.

Boston City Hospital.

11. Killian, Hans: The Use of Coramin for Combating Poisoning from Narcotics and Hypnotics, from an Experience of over 200 Cases, Anesth. & Analg. **14**: 23 (Jan.-Feb.) 1935.
12. Haggard, H. W., and Greenberg, L. A.: Antidotes for Strychnine Poisoning, J. A. M. A. **98**: 1133 (April 2) 1932.
13. Weiss, Soma: Indications and Dangers of the Use of Barbituric Acid Derivatives, Am. J. M. Sc. **188**: 729 (Nov.) 1934.
14. Raginsky, B. B., and Bourne, Wesley: The Action of Ephedrine in Avertin Anesthesia, J. Pharmacol. & Exper. Therap. **43**: 209 (Sept.) 1931. Moritsch, P.: Ueber die Wirkung von Weckmitteln auf die Basisnarkose, Arch. f. exper. Path. u. Pharmakol. **168**: 249, 1932.
15. Purves-Stewart, James, and Willcox, William: Cisternal Drainage in Coma from Barbitone Poisoning, Lancet **1**: 500 (March 10) 1934.

ABSTRACT OF DISCUSSION

DR. CHAUNCEY D. LEAKE, San Francisco: Is there any clinical advantage in utilizing the difference of action in drugs, such as the salicylates, which act by virtue of pulling fluid out of congested areas, and those, such as the morphine derivatives, which depress sensory pain perception? The first type would seem preferable in congestive pain, while the second would seem more useful in traumatic pain.

DR. SOMA WEISS, Boston: The difference in relieving pain with the aid of various types of analgesics is difficult to evaluate from clinical experience. All one can say is that in milder pain, especially the neuralgic type, salicylates or the acetophenetidin group may be very useful. In more severe pain my associates and I are using members of the morphine group. Whether any differentiation can be made in clinical medicine on the basis of pharmacologic action, I am not certain. In connection with this question I wish to emphasize once more that if the patient has pain and as a result suffers from sleeplessness, he may continue to be disturbed for weeks when hypnotics alone are administered, but when hypnotics such as the barbituric acid derivatives are combined with analgesics such as codeine one-half grain (0.03 Gm.) and, in addition, with an average dose of salicylates or acetophenetidin, remarkable improvement in sleep and the disappearance of the pain may result. Therefore, I believe that the intelligent and skilful combination of hypnotics and analgesics has a distinct place in medicine.

PRIORITY AMONG AMERICAN PHYSICIANS IN DEMONSTRATING THE CAUSE OF GRAIN ITCH

TARDY CREDIT THEREFOR GIVEN TO DR. LYMAN TALMAGE RAWLES

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Several years ago, in collecting medical and entomologic data for a professional paper, I[1] incidentally acquired the suspicion that, owing to certain unfortunate omissions and errors for which the orginal investigator himself was only partly responsible, credit for priority among American physicians in demonstrating the cause of grain itch had been given to the wrong men. Careful investigation, by way of literary research, correspondence and personal interview, transformed the suspicion into a firm conviction. I resolved that, when time permitted, I would review the relevant facts and give "credit where credit is due." Hence this paper.

HISTORY OF DERMATITIS FOLLOWING CONTACT WITH GRAIN OR STRAW, AND OF AN APPARENTLY ASSOCIATED MITE

It would lead quite beyond the scope and the scientific requirements of this paper to reproduce here in detail the vague and shadowy history of the dermatitis and of the apparently associated mite that, during the eighty years preceding 1909, intermittently engaged the troubled attention of laymen and the puzzled attention of physicians in Europe and America. That history has already been presented in sufficiently full outline by Webster,[2] Schamberg,[3] Rawles,[4] Stelwagon and

1. Kittredge, H. E.: Grain Itch—Report of Two Cases Occurring in a Small Epidemic, Virginia M. Monthly **60**: 357 (Sept.) 1933.
2. Webster, F. M.: (*a*) A Predaceous and Supposedly Beneficial Mite, Pediculoides, Becomes Noxious to Man, Ann. Entomologic Soc. of America **3**: 15 (March) 1910; (*b*) A Predaceous Mite Proves Noxious to Man, circular 118, Bur. Ent., U. S. Dept. Agriculture, April 23, 1910.
3. Schamberg, J. F.: Grain Itch (Acarodermatitis Urticarioides): A Study of a New Disease in This Country, J. Cutan. Dis. **28**: 67 (Feb.) 1910.
4. Rawles, L. T.: Dermatitis Pediculoides Ventricosus; Synonym, Grain Itch, Indiana State M. J. **3**: 351 (Sept. 15) 1910.

Gaskill [5] and others. It is therefore necessary to sketch here so much only of the history referred to as is requisite to a clear understanding of the subsequent sections of this paper.

History in Europe.—Dermatitis in laborers who had handled sacks of wheat or barley, or who had been in contact with the straw of those cereals, was observed by Lagreze-Fossat and Montane in France in 1849, by Robin in that country in 1867 and 1872, by Targioni-Toizzetti in Italy in 1875, by Geber in Hungary in 1879, by Koller in the same country in 1882 and by Flemming in Germany in 1884.[6]

Webster stated that the cases observed by Lagreze-Fossat and Montane and by Robin were due to Pediculoides [Acarus] tritici Lagreze-Fossat (1851) and that it "would seem quite probable" that the mite involved in the cases described by Geber was Pediculoides ventricosus Newport (1850). As to the cases observed by Koller and Flemming in Hungary and in Germany, respectively, Webster was less certain; but, since the Angoumois grain moth (Sitotroga cerealella), hereinafter shown to be a frequent host of Pediculoides ventricosus, is a very common pest in those countries, he suspected that the same mite was responsible.

Lastly, at the tenth meeting of the Italian Dermatologic Association, held in Rome in December 1908, Ducrey [7] and Sberna [8] presented papers showing that a certain epidemic of dermatitis was caused by Pediculoides ventricosus in wheat.

History in America.—American observations of dermatitis following contact with straw antedate the European. An itching eruption in persons who had slept in barley straw beds was noted in Massachusetts in 1829, 1831 and 1845, and in New York in 1879. There was no suspicion that a mite was responsible for the condition, the cause being assigned to certain grain parasites easily visible to the naked eye, such as Meromyza americana and Isosoma hordei, hereinafter mentioned as hosts of Pediculoides ventricosus. In much the same way as malarial fever was attributed to the "night air" itself, not to the plasmodium carried by mosquitoes in that air, so the dermatitis was attributed to the wholly innocent parasites of the wheat and the barley. And why not? For when the infesting Meromyza and Isosoma were burned with the straw, the dermatitis disappeared!

First American Clinical Observation of the Mite.—According to Webster,[2] the first American observation of Pediculoides itself in connection with the malady was made by Dr. Henry Skinner of Philadelphia about 1894 or 1896. The owner of a suburban boarding house, many inmates of which had been attacked by a "rashlike disease," supposed to have been contracted from their beds, submitted straw dust and débris from the mattresses of the suspected beds. On examination, Dr. Skinner found specimens of the mite. No further investigation was made.

First Clinical Description of the Dermatitis.—The next important event in the history of the condition occurred in 1901, when Schamberg [9] gave the first clinical description, in a paper entitled "An Epidemic of a Peculiar and Unfamiliar Disease of the Skin." That contribution, although admirably crystallizing the previous vague and fragmentary accounts of the malady into a definite clinical entity recognizable by physicians, failed to assign a parasite or other agent to the etiologic rôle.

History and Description of the Mite.—In 1849 Mr. George Newport [10] of England discovered in the nest of a wasp (Anthophora retusa) at Gravesend a mite that he called Heteropus ventricosus, describing it in a paper read before the Linnaean Society of London, March 5, 1850, and published, according to Kappel,[11] on October 18 of the same year. As the genus Heteropus was preoccupied, Targioni-Toizzetti,[12] in 1875, substituted the generic name Pediculoides; hence the present entomologically recognized nomenclature, Pediculoides ventricosus Newport (1850).

It is, according to Banks,[13] a true mite, of the class Arachnida, order Acarina, superfamily Sarcoptoidea, family Tarsonemidae, genus Pediculoides. Its synonyms, as listed by Carazza,[14] are Heteropus ventricosus Newport, 1850; Acarus tritici Lagreze-Fossat, 1851; Physogaster larvarum Lichtenstein, 1868; Sphaerogyna ventricosa Laboulbene e Megnin, 1885; Pediculoides tritici Targioni-Toizzetti, 1878.

It should be pointed out that, although Reuter [15] cited Pediculoides ventricosus Newport (1850) as a good species and made no mention of Acarus tritici Lagreze-Fossat (1851), and that although Carazza [14] named not only the latter but nearly all of the other alleged itch-producing grain mites as synonyms of Pediculoides ventricosus Newport (1850), there is still some doubt whether the latter is the only grain-infesting mite capable of causing grain itch. Thus Banks [16] in 1909, reporting on the Pediculoides that Schamberg and Goldberger had proved to be the cause of the disease in the cases studied by them, stated not that the incriminated mite was Pediculoides ventricosus Newport (1850) but that it was "very close to, if not identical with, the Pediculoides ventricosus."

With this and similar doubt-inspiring statements in mind, I recently appealed to Dr. H. E. Ewing of the Bureau of Entomology, than whom there is in the United States no higher authority on Acarina. Dr. Ewing responded as follows:

> The only points in regard to the identity and proper scientific name of the American grain itch mite that I care to pass upon are the following:
>
> 1. All specimens of Pediculoides that I have examined, taken from man as suspected of attacking man, are Pediculoides ventricosus (Newport).
>
> 2. I have never been able to separate Pediculoides [Acarus] tritici Lagreze-Fossat from Pediculoides ventricosus (Newport). However, having never seen the types of either, I am in no position to say that they are the same.
>
> I hope some European worker can straighten out the confusion existing between these species. It is a more fitting problem for one of them.

This frank and authoritative pronouncement leaves the matter in much the same status as before: The mite

5. Stelwagon, H. W., and Gaskill, H. K.: A Treatise on Diseases of the Skin, ed. 9, Philadelphia and London, W. B. Saunders Company, 1923, pp. 1242 (footnote), 1243 (footnote).
6. These authors were cited by Webster.[2a]
7. Ducrey, A.: Acariasi da grano, in forma epidemica, dovuta al Pediculoides ventricosus (con presentazione di preparati di acari), Gior. ital. d. mal. ven., Milano **50**: 97, 1909.
8. Sberna: Telle Dermatosi accidentale da acari della tignole del grano (pediculoides ventricosus), Gior. ital. d. mal. ven., Milano **50**: 126, 1909.
9. Schamberg, J. F.: An Epidemic of a Peculiar and Unfamiliar Disease of the Skin, Philadelphia M. J. **8**: 5 (July 6) 1901.
10. Newport, George: Further Observations on the Habits of Monodontomerus, with Some Accounts of a New Acarus, Heteropus Ventricosus, a Parasite in the Nests of Anthophora Retusa, Proc. Linn. Soc. London (November 1848-June 1855), (42) **2**: 70.
11. A. W. Kappel in 1896a gives the date of issue of No. 42, which contains Newport's article, as Oct. 18, 1850. According to this, the specific name ventricosus Newport, 1850, would have priority by a year over tritici Lagreze-Fossat, 1851.
12. Targioni-Toizzetti, cited by Schamberg.[3]
13. Banks, Nathan, quoted by Schamberg.[3]
14. Carazza, D.: Parassitologia animale, ed. 2, 1922.
15. Reuter, Enzio: Acta Societatis Scientiarum Fennicae **36**: 185, 195, 1909.
16. Banks, Nathan, quoted by Schamberg and Goldberger.[17]

described by Newport [10] causes grain itch; but whether it is the same mite that Lagreze-Fossat described a year later and, therefore, whether a mite that causes grain itch should be invariably called Pediculoides ventricosus Newport, are still uncertain. However, following the established American usage, the entomologic nomenclature employed in this paper as connoting the cause of grain itch will be Pediculoides ventricosus Newport.

This Pediculoides was recognized and entomologically identified, probably for the first time in America, by Webster [2] in 1882, while investigating, in southern Illinois, the ravages of the Angoumois grain moth, a frequent host of the mite. The latter, however, as indicated by Webster,[2] was doubtless abroad in the land "as early as 1830 [1829]," or twenty years before it was discovered in England.

Pediculoides ventricosus Newport is parasitic on the Angoumois grain moth (Sitotroga cerealella); on the wheat joint worm ([Harmolita] Isosoma tritici Fitch); on the wheat straw-worm (Harmolita grandis Riley); on the Ditropinotus aureoviridis Crawford (a hymenopterous insect known as a chalcid fly, and itself parasitic on the wheat jointworm, the wheat strawworm and the like); on the larvae of Bruchus, infesting peas in Italy; on Meromyza americana, infesting the stems of wheat; on the barley jointworm (Isosoma hordei); on Leptotrachelus dorsalis, infesting wheat; on the periodic cicada (Cicada septemdecim); on the peach twig borer (Anarsia lineatella); on the cotton boll weevil (Anthonomus grandis) and the pepper weevil (A. eugenii); on wood-boring beetles, and on other soft-bodied insects and their larvae.

While this enumeration of the varied hosts of Pediculoides is of interest, as accounting for the far-flung incidence of the dermatitis of which it is now known to be the cause, it is with its activities as a parasite of the Angoumois grain moth, especially in the eastern part of the United States, and of the wheat jointworm in the midwestern states east of the Mississippi, that I shall be particularly concerned in the next section of this paper.

AMERICAN DEMONSTRATIONS THAT THE DERMATITIS FOLLOWING CONTACT WITH GRAIN OR STRAW IS CAUSED BY PEDICULOIDES VENTRICOSUS

The Work of Schamberg and Goldberger.—In the spring of 1909 an outbreak of the same "peculiar and unfamiliar disease of the skin" that was described by Schamberg [9] eight years before occurred among the crew of twenty sailors of a private yacht docked in the Delaware River at Philadelphia. Cases among the crews of other craft, and seventy cases in twenty separate households and boarding houses, brought the total number of victims to 123. The epidemic attracted the attention not only of the local health authorities of Philadelphia but of the federal government. The surgeon general of the United States Public Health and Marine Hospital Service ordered Passed Assistant Surgeon Joseph Goldberger of that service to Philadelphia to make an investigation of the malady, which he did in cooperation with Dr. Schamberg.

In nearly every case studied it was shown that the patient had been in contact with a new mattress made of wheat straw that had been received in small part from Indiana, but for the most part from southern New Jersey. The significance of these observations will become more clearly apparent in detailing the work of Rawles in Indiana and in pointing out the credit due him. It is sufficient here to state that investigations by the United States Bureau of Entomology revealed the fact that, while nearly all the wheat straw on which Schamberg and Goldberger worked was infested with the Angoumois grain moth, only a small proportion harbored the wheat jointworm. Both of these parasites, however, are hosts of Pediculoides ventricosus — the grain moth being the predominant wheat pest in New Jersey; the jointworm, in Indiana.

It is unnecessary to review in detail Schamberg and Goldberger's investigations, the admirable thoroughness and scientific conclusiveness of which are not in question. They demonstrated the invariable presence of a mite in the straw from which the dermatitis was contracted, and they reproduced the dermatitis by exposing the human skin to the mite. The latter, as stated in the preceding section, was identified by Mr. Nathan Banks,[16] a noted expert on Acarina, Bureau of Entomology, not as Pediculoides ventricosus Newport but "as very close to, if not identical with, the Pediculoides ventricosus."

The investigators made no mention of having recovered Pediculoides from a lesion of the dermatitis.

Schamberg and Goldberger [17] began their work June 9, 1909, submitted a preliminary report of their observations June 21 and published that report July 9. A final or subsequent report, in no essential modifying the preliminary account, was published by Goldberger [18] June 10, 1910.

Since the preceding publications, such of the standard dermatologic textbooks as have treated of grain itch at all have either credited Schamberg and Goldberger as the sole discoverers of the cause of the disease or, if mentioning the work of Rawles, have given credit for priority of discovery to Schamberg and Goldberger. Only one treatise, that of Stelwagon and Gaskill,[19] as far as I have observed, has approached a just presentation of the facts. That volume stated: ". . . Goldberger and Schamberg, *and, almost simultaneously, Rawles,* were the first to associate convincingly cause and effect, and to identify the organism; Schamberg's investigations being extensive and conclusive." (The italics are mine.)

The Work of Rawles.—Approximately one month before Schamberg and Goldberger commenced their investigation of the epidemic of dermatitis in Philadelphia and its environs, another epidemic of the same disease began in the general section embracing northern Indiana. Sixty-one cases were studied by Dr. Lyman Talmage Rawles, an ambitious young man who had graduated four years previously from the Fort Wayne Medical College and who had settled in Huntertown, a small country village ten miles north of Fort Wayne. That Dr. Rawles was imbued with the scientific spirit is evidenced by the fact that he was equipped with a microscope and accessories, rare implements in the armamentarium of the country doctor of over a quarter-century ago.

It will, I think, the more effectively subserve the interests of clarity, in endeavoring to point out the credit that is due to Rawles [20] as the original and independent American discoverer of the cause of grain itch,

17. Schamberg, J. F., and Goldberger, Joseph: Epidemic of an Urticarioid Dermatitis Due to a Small Mite (Pediculoides Ventricosus) in the Straw of Mattresses, Pub. Health Rep. **24**, Nos. 27-53 (July-Dec.) 1909.

18. Goldberger, Joseph: The Straw Itch (Dermatitis Schambergi): A Disease New to American Physicians, Pub. Health. Rep. **25**: 779 (June 10) 1910.

19. Stelwagon, H. W., and Gaskill, H. K.[5] (footnote p. 1242).

20. Rawles, L. T.: Dermatitis Ditropinotus Aureoviridis; Synonym, Straw Itch, Indiana M. J. **2**: 337 (Aug. 15) 1909.

if I first present his own account of his etiologic investigations, supplying later such omissions of dates, names and particulars as will give to that account the significance and importance that it deserves. He stated:

In May 1909 a very strikingly strange skin disease presented itself in this and surrounding country in epidemic form . . . limiting itself to the wheat growing sections.

The people generally affected were farmers and those living in small villages or towns where straw is used in beds, under carpets and around stables to bed stock. . . . The following incident led to an investigation as to the probable etiology:

A family had cleaned house, refilling the straw ticks of their beds and placed fresh straw under the carpets, and in about one week the family had developed this peculiar skin disease. In the beds was found a small, black fly, about the size of an ordinary gnat, which at first it appeared to be, but closer observation revealed that it was not of the gnat family. Upon examination of the straw it was found that a large number of the straws were perforated . . . through the bark of the straw, in the region of the joint, generally about two inches from the joint. The perforations were about the size of a small pinhole and ranging in number from ten to thirty in a straw. Upon section of the straw a small black fly was found under many of the openings through the bark.

Several flies were examined to ascertain if they possessed a piercing proboscis, and while observing one which had just been taken from under the bark of the straw, through which there was no perforation over the fly, a small mite was observed crawling over the dead body of the fly.

Placing the bodies of several flies under the microscope and using a ¼-inch objective and a No. 5 eyepiece, it was found that on nearly all flies over which the bark was intact a small parasite could be detected, these mites varying in number from two to four mites to each fly. Upon furthering the observations it was found that the dermatitis lasted after the flies had been observed and exterminated.

The following experiments were tried to prove whether it be the fly or the parasite that was the etiologic factor in producing the dermatitis:

Six live flies were taken, upon which no parasite could be found; these were placed under a watch glass and bound upon the right arm, leaving them in contact with the skin for three hours. Upon the left arm four dead flies, on which living parasites had been observed, were placed under a watch glass and left in contact with the skin for three hours, after which the glasses were removed and results awaited. The right arm showed nothing. Upon the left arm there appeared within twelve hours four small wheals, the character and evolution of which are later described.

To further experiments some fresh lesions of patients were scraped and the scrapings examined microscopically and two of the mites were found in the scrapings.

It is doubtful whether any other account of a medical investigation as succinct and straightforward as the preceding ever more completely failed to achieve what should have been its instant result; namely, to win credit for its author as the original and independent American discoverer of the cause of the disease concerned. Fortunately, however, the several specific names and dates which, inserted in the account, would have ensured its accomplishment of this are still available in Dr. Rawles's professional files.

Before presenting these data, so naively omitted by Rawles, it is necessary to introduce a few entomologic facts in order to make more intelligible the description of certain of Rawles's observations, such as the perforated straws, the mite-bearing "flies," and the like, and to the end that subsequent references to those features may be clearly understood.

There are several parasitic pests of wheat, but it is with only one of these, the wheat jointworm (Harmolita) Isomoa tritici Fitch, with which we are here concerned. This parasite, an insect, has four stages—egg, larva, pupa, adult. As an adult it is a black fly about three-sixteenths inch long and looks somewhat as would an ant with wings. The egg is pushed down into the stem of the wheat plant with the ovipositor of the female, in May, passes through the stages of larva and pupa, and, the following May, having become an adult, gnaws a tiny circular hole, from within outward, through the side of the wheat stem, and, in a free environment, flies away in search of growing wheat, in which to initiate another life cycle.

These entomologic facts explain (1) the "perforations" in the straws, and (2) "the small black flies" in the straw-ticks of the beds, described by Rawles.[20] But they do not explain the far more important third factor noted by him—"the small mites crawling over the dead bodies of the flies," later reproducing the dermatitis, and still later recovered from the lesions of patients. This third factor is as readily accounted for as were the first and the second factors. Where straw is kept in a mass, as in a stack, a mow, a bale, or a bed-tick, Pediculoides ventricosus literally swarms through the mass, and when, in May, the adult jointworms begin to gnaw openings in the straw, the mites—many, many times smaller than the jointworms—enter through the beginning openings and kill all but about 5 per cent of the jointworms before the latter can enlarge the openings sufficiently to escape. This accounts for the third factor, the mites.

It now remains but to supplement Rawles's [20] original account with the specific names and dates previously mentioned to complete the detailed record of the original and independent American discovery of the cause of grain itch. Those names and dates [21] are embodied in the following paragraph:

In the spring of 1909, there lived at Huntertown a Mrs. Porter. Residing in the same house with her were her son and her son-in-law and his wife, Mr. and Mrs. Bert Darrow. During the week preceding April 26th, Mrs. Porter "cleaned house," refilling the bed-ticks with, and placing under the carpets, fresh wheat straw from a stack in her back lot. In so doing, Mrs. Porter contracted a "cold"; and, on April 26th, Dr. Rawles was summoned to her. On May 11th, Mr. Darrow came to Dr. Rawles's office with a skin eruption that the latter at first thought was urticaria. The patient stated that his wife, who had remained at home, was suffering with the same affection. Dr. Rawles prescribed for both. The next day Mr. Darrow, meeting Dr. Rawles on the street, told him that he (Darrow) and his wife were no better, and that his mother-in-law (Mrs. Porter) and his brother-in-law had the same disease. Two days later Mr. Darrow again came to Dr. Rawles's office, when scrapings, taken from lesions on the patient's back and microscopically examined by Dr. Rawles, showed the presence of mites. The patient remarked that since the new straw was put under the carpets at Mrs. Porter's the house had been "full of small flies," and he wondered whether the straw had anything to do with the flies and the "itch" with which all in the house were suffering. On the same day, Dr. Rawles and Mr. Darrow obtained from the stack in the back lot of Mrs. Porter's home specimens of the straw that had been put under the carpets, etc. With mite-bearing flies obtained from this straw, the etiologic investigations described in Dr. Rawles's [20] original paper were carried out.

Thus, on May 14, 1909, twenty-six days before Schamberg and Goldberger began their joint investiga-

21. Furnished in personal communications from Dr. Rawles.

tion, thirty-eight days before they submitted the preliminary report of their observations, and fifty-six days before they published that report, Rawles recovered mites from lesions of grain itch and reproduced those lesions by exposing the skin to the same mites.

Having confirmed, by repeated experiments on several other patients, during the week following May 14, the discoveries made on that date, Rawles's next step was to obtain an identification of the mite that he had proved to be the cause of the dermatitis. Accordingly, specimens of the straw with which he had been working, and which were known to contain the "flies" and the incriminated mite, were sent to the Department of Entomology, Purdue University, Lafayette, Ind., with explicit information as to the nature of the identification desired and as to the procedure which, in the light of the personal experience of Rawles in examining those particular specimens, was most likely to lead to success at the hands of the examining entomologist.

Here was an opportunity fraught with the highest importance, not only to Rawles but to many thousands of his fellow men. For eighty years the inhabitants of the grain-growing sections of America and Europe had been intermittently scratching; thousands of farm hands, of threshers, of handlers of grain, of the crews of water-craft, had been made miserable; boarding houses had been emptied of their inmates, and whole cargoes of cereals had been dumped into the water that those on board might be freed from a pestiferous dermatitis. The culprit mite at last had been captured, tried and found guilty; its sentence was only being postponed for want of a name. Dr. Rawles impatiently awaited the decision of the entomologic high court at Purdue. In a few days, the decision came and was as follows:[20]

> The straws you sent are infested with the wheat-straw worm (Isosoma tritici), which gets inside of the main stem. The parasite which is working up on the fly is the ditropenotus aureoviridis. This is a new species of parasite, it having been described last year for the first time.

So the name of the convicted criminal was "ditropenotus aureoviridis"—surely too euphonic, even when misspelled in lower case, for a creature so vile!

As to the report as a whole, it is well to note, not in the spirit of pedantry but in that of science, that the straw was not "infested with the wheat-straw worm [i. e., the wheat straw-worm, Harmolita grandis Riley]" but with the wheat jointworm (Harmolita) Isosoma tritici Fitch, and that "the ditropenotus aureoviridis [Ditropinotus aureoviridis Crawford]"[22] was not "described last year [1908] for the first time" but in 1907.

In reading this report, scientifically inaccurate though it is, I realized that its incrimination of Ditropinotus aureoviridis as the cause of grain itch nevertheless pointed to the possibility that that dermatitis is not an etiologic entity but is due now to Ditropinotus, now to Pediculoides. Deciding to clear this point at first hand, I procured from the Bureau of Entomology living specimens of Ditropinotus auroeoviridis Crawford, just as they were emerging in the adult, or fly stage, from the "cells" of the wheat jointworm, late in July 1933, and confined eleven of them on the flexor surface of my bare left forearm, under a small inverted Petri dish, for six hours. Not even the slightest irritation resulted. It was evident that Ditropinotus aureoviridis Crawford does not cause grain itch.

It did, however, cause several suspicions — among them the suspicion that the examining entomologist at Purdue did not see Ditropinotus. Rereading the letter from the chief of the Bureau of Entomology, dated July 18, stating that the specimens of Ditropinotus would be furnished, I noted the sentence "At the time this material is sent you, I shall also indicate the approximate date the adults may be expected to emerge from the jointworm cells." They did not emerge until ten days later, or July 28. Investigation revealed that this was evidently the second seasonal generation of the parasite, the first generation beginning to emerge, in this latitude, "about the first week in June." Even so, I wondered why Ditropinotus should refuse to emerge for a dermatologist in subtropical Washington before the first week in June but obligingly appear for a general practitioner and an entomologist in chilly northern Indiana at least two weeks earlier, or May 14, the date on which Rawles first saw the alleged Ditropinotus "crawling over the dead body of the fly." For, be it noted, if the entomolgist at Purdue saw Ditropinotus on or about May 25, Rawles must have seen it May 14; for the two were looking at the same object, in the same situation—a parasite on a fly. Investigation of the seasonal habits of Ditropinotus, supplemented by correspondence with the Bureau of Entomology, Washington, and with the state agricultural experiment stations of Kentucky, Ohio, Illinois and Indiana, elicited the following facts: The eggs of Ditropinotus aureoviridis are deposited in the cells of the jointworm; the resulting larvae, full grown, pass the winter in the cells, beginning to emerge as adults (flies) "about the first week in June," in Virginia; between June 16 and June 27 in Kentucky; from "just prior to harvest" to "before fall" in Ohio, and from July 24 to August 30 in Illinois, and while there are "no [official state] records of the emergence of the Ditropinotus aureoviridis" in Indiana. Wildermuth, for the U. S. Bureau of Entomology, did find not only the latter insect but the wheat jointworm, both being parasitized by Pediculoides ventricosus, in straw in Rawles's barn, at Huntertown, in December.

Thus it became clear, on the recorded testimony of competent entomologists, that even in Virginia, approximately 150 miles farther south than Huntertown, Ind., the adult Ditropinotus does not emerge before the first week in June; that in Kentucky, in the same latitude as Virginia, it does not emerge until after the middle of June; that in Ohio and Illinois, in the same latitude as Indiana, it does not appear earlier than "just prior to harvest," and that in Indiana itself there is no official record of its emergence in spring, summer or fall. Therefore, it is highly improbable, if not impossible, that the "fly" in question was seen either at Huntertown on May 14 or at Purdue about May 25.

Nor are the preceding facts the strongest available evidence that the examining entomologist did not see Ditropinotus. Just eight words of his report convict him "out of his own mouth." Those words are: *"The parasite which is working upon the fly. . . ."* (The italics are mine.) The "parasite" does not work "upon the fly." The adult Ditropinotus fly does not work upon the adult jointworm fly. The larva of Ditropinotus works upon the larva of the jointworm. "The larva," said Phillips and Poos,[23] "feeds almost continuously, if undisturbed, until nothing remains of the host larva but the empty skin." That is, when the Ditropinotus larva has finished with the jointworm larva there is

22. Crawford, J. C.: New North American Hymenoptera, J. New York Entomologic Soc. **15**: 178, 1907.

23. Phillips, W. J., and Poos, F. W.: Life-History Studies of Three Joint Worm Pasasites, J. Agric. Research **21**: 412 (June 15) 1921.

nothing left—no adult jointworm fly develops. It is like the small boy eating the apple: "There ain't go'n' ta be no core!" Consequently, as far as Ditropinotus is concerned at all, the examining entomologist's report "The parasite which is working upon the fly is the ditropenatus aureoviridis" can be interpreted only as follows:

"The straws that you sent are infested with wheat jointworms that have never been attacked by Ditropinotus aureoviridis."

If, then, the parasite at work upon the fly was not Ditropinotus aureoviridis, what parasite was it? Since the straws sent to Purdue were from the same stack as those that Rawles had been studying; since the presence of both "flies" and mites in the straws was verified by Rawles just before the straws were sent; since the mites that Rawles saw "crawling over the dead bodies of the flies" were the same as those that he recovered from the lesions of Mr. Bert Darrow and other patients with grain itch, and the same as those with which he reproduced the disease, and since the only parasite known to be capable of causing grain itch is Pediculoides ventricosus, the parasite seen at Purdue about May 25, 1909, must have been Pediculoides ventricosus.

Indeed, this conclusion is confirmed in a personal communication recently received from Prof. J. J. Davis, the present chief in entomology at Purdue, who states that the parasite was "apparently . . . misidentified," and who quotes Webster [24] to the same effect, as follows:

> Owing to an unfortunate misunderstanding, for which no one connected with these investigations [by the U. S. Bureau of Entomology] is responsible, Dr. Rawles did not receive a proper determination of the mite. . . . The entomological nomenclature in his paper . . . should therefore be corrected by substituting Pediculoides ventricosus for Ditropinotus aureoviridis wherever the latter name occurs. . . .

This gratifying announcement was no surprise to Rawles; for when Wildermuth, investigating for the bureau, visited Rawles at Huntertown in December 1909 and showed him Pediculoides ventricosus in straw from his own barn, Rawles instantly recognized that mite as identical with the one which he had recovered from the lesions of Mr. Bert Darrow and other sufferers from grain itch, and with which he reproduced the disease on the preceding May 14.

And when Webster showed Schamberg [3] the mite found at Huntertown by Wildermuth, Schamberg recognized it as identical with the one found by him and Goldberger at Philadelphia and identified by Banks [16] as "very close to, if not identical with, the Pediculoides ventricosus."

There is no certainty of the date on which Pediculoides was misidentified for Rawles, but careful investigation points to May 25. Equally uncertain is the date on which Rawles submitted the manuscript of the account of his discoveries to the *Journal of the Indiana State Medical Association,* in which it was published on Aug. 15, 1909. In the absence of any record, the editor's statement that the manuscript probably was received in June may be accepted as correct.

Nor does the date on which the manuscript was submitted, or the date on which the mite was misidentified, greatly matter. The significant facts remain that on May 14, 1909, twenty-six days before Schamberg and Goldberger began their joint investigation, Rawles recovered from lesions of grain itch a mite with which he reproduced that disease and which was subsequently identified by Wildermuth and Webster [2] as Pediculoides ventricosus.

Rawles did his work—original and independent—in a small country village, without laboratory facilities, and, as is evident, far removed from those with entomologic knowledge and technical skill adequate to aid him, while Schamberg and Goldberger [17] worked in a great metropolitan medical center, with the well-nigh limitless resources of the United States Public Health and Marine Hospital Service and the United States Bureau of Entomology at their command.

RAWLES'S INCIDENTAL CONTRIBUTION TO ENTOMOLOGY

Nearly as notable as his discovery of the cause of grain itch was Rawles's incidental contribution to one of the problems of entomology.

I pointed out in an earlier section that the predominance of the Angoumois grain moth as a wheat pest in the Eastern states and as a host of Pediculoides ventricosus accounted for the origin, in the straw studied by Schamberg and Goldberger, of the epidemic of grain itch in the East. However, this threw no light on the origin of the widespread epidemic being investigated by Rawles, for the reason that the grain moth never occurs in great abundance in the Middle West except in grain kept in store in southern sections of Indiana and Illinois. Commenting on the effect of Rawles's discoveries in helping to solve this entomologic problem, Webster stated: [24]

> Dr. Rawles' investigations were very carefully made and the results are exceedingly valuable for the reason that, in case of this western epidemic, he was able to trace the cause of the dermatitis to Pediculoides ventricosus and follow this back to the host insect, Isosoma tritici. This paper of Dr. Rawles . . . not only clears up the obscurity with reference to the cause of this epidemic in the Middle West . . . but, furthermore, these studies seem to solve the problem of the cause of the skin eruption noticed by Dr. Harris to have occurred as far back as 1830 [1829].

Thus Rawles, in proving that Pediculoides ventricosus, parasitic on the wheat jointworm, was the cause of the Midwestern epidemic of grain itch, demonstrated incidentally first, to entomologists, that the wheat jointworm was the predominant wheat pest of the corresponding region and secondly, to physicians, that the itching eruption noted eighty years before, in persons who had slept in beds of barley straw infested with the barley jointworm, probably was grain itch, caused by Pediculoides ventricosus, twenty years before that villainous mite was discovered.

CONCLUSIONS

1. The earliest observation of dermatitis following contact with straw or grain—probably what is now known as grain itch, caused by Pediculoides ventricosus—was made in Massachusetts, in 1829.[25]

2. The mite that is now entomologically known as Pediculoides ventricosus Newport [10] (1850) was discovered by Mr. George Newport of England in 1849 and was described by him as Heteropus ventricosus in 1850.

3. Pediculoides ventricosus was first entomologically identified in the United States by Webster [2] in 1882.

4. Pediculoides ventricosus apparently was first observed in the United States, in connection with what is now known as grain itch, by Dr. Henry Skinner [26] of Philadelphia, about 1894-1896.

24. Webster, F. M.,[2b] p. 17 (footnote).

25. Stelwagon, H. W., and Gaskill, H. K.,[5] p. 1243 (footnote).

26. Skinner, Henry, cited by Webster.[2]

5. The first clinical description of what is now known as grain itch was published by Dr. Jay Frank Schamberg,[9] July 6, 1901, under the title "An Epidemic of a Peculiar and Unfamiliar Disease of the Skin."

6. It is still uncertain whether Pediculoides ventricosus Newport[10] (1850) is the only grain-infesting mite capable of causing grain itch.

7. Pediculoides ventricosus was first recovered from a lesion of grain itch, at any rate in the United States, by Dr. Lyman Talmage Rawles, on May 14, 1909.

8. The first American demonstration that Pediculoides ventricosus is the cause of grain itch was made by Dr. Lyman Talmage Rawles on May 14, 1909.

9. The second American demonstration that Pediculoides ventricosus is the cause of grain itch was made by Drs. Jay Frank Schamberg and Joseph Goldberger[17] between June 9 and June 21, 1909.

10. Dr. Lyman Talmage Rawles was the original and independent American discoverer of the cause of grain itch.

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ACUTE COMPLETE GRANULOPENIA WITH DEATH DUE TO DINITROPHENOL POISONING

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There have been reports recently of ingestion of alpha-dinitrophenol (1-2-4) with subsequent psychic disturbances, vasomotor and circulatory changes, dermatitic reactions[1] and even an otologic complication.[2] To date only three cases of agranulocytic angina following ingestion of dinitrophenol have been reported.[3] In one case,[4] in which the drug was self administered for two weeks in doses of 100 mg. four times daily, the patient recovered following withdrawal of the drug, roentgen therapy and the use of pentnucleotide. The second patient, taking 21,800 mg. in the form of "Nitraphen" over a period of four months, developed a picture of complete granulopenia with unfavorable reactions, such as sense of warmth, perspiration, fatigue, sore throat, vertigo and a pruritic eruption of the skin. These symptoms vanished in about three weeks following withdrawal of the drug but recurred with the repetition of the drug. This patient responded to pentnucleotide and blood transfusion.[5] In the third case,[6] 90 grains (5.8 Gm.) had been taken in a period of twenty days and subsequently nausea, diaphoresis, pyrexia and scleral icterus occurred, with ulceration of the pharynx, inflammation of the nasal and pharyngeal mucosa and of the gums and cervical adenopathy. The patient, under administration of leukocytic cream and pentnucleotide, began to show a response at the end of the third day of treatment and was later discharged improved. Tainter and Wood[7] describe in detail a case reported by Geiger[8] in a short communication: A physician, informed of the effects of the drug, took a dose approximately seventeen times the recommended therapeutic or subfebrile dose of dinitrophenol. Restlessness, apprehension, progressive rise in temperature to 105.7 F., rapid pulse, profuse perspiration, delirium and, finally, coma and death characterized the eleven-hour course of the clinical picture. No blood count was reported nor was postmortem study of the bone marrow described.

In a series of eighteen cases of the ingestion of dinitrophenol reported by Masserman and Goldsmith,[9] who tried to evaluate the psychobiologic changes in schizophrenic patients by use of the drug, none of the blood pictures showed any change in cytology. This series includes one death from the administration of the drug but with no hematologic or bone marrow changes. In a series of 113 cases treated for obesity, no anginal symptoms followed the use of the drug. Blood studies were not reported.[10]

Because of the increasing number of deaths reported in the recent literature following the use of a drug the toxicity of which is still a matter of conjecture and because of the protean manifestations of this toxicity, we herewith submit the following report:

REPORT OF CASE

History.—A Jewish girl, aged 13 years, was referred by Dr. J. M. Leavitt on July 1, 1934, at 7:30 p. m., with the following history: The patient had been taking dinitrophenol in 1½ grain (0.1 Gm.) capsules, one daily since May 15, at which time she weighed 265 pounds (120 Kg.). She had received 100 capsules from her family physician on May 15, with instructions to take one capsule daily. In a period of forty days the patient had lost 25 pounds (11 Kg.). By June 30, forty-six days later, only forty-six remaining capsules were found. At this time the patient began to complain of weakness, malaise, feverishness and sore throat and she began to vomit. On examination the patient, who had been in syncope, appeared asthenic and was delirious and occasionally euphoric. The head and face were warm. Respiration was irregular. The knee jerks were absent. Positive Murphy signs were present bilaterally. Submucous hemorrhages were seen on the soft palate, as were small areas of necrosis on the tip of the uvula and slight edema of the peritonsillar fossa. The tongue was dry, there was marked fetor oris and the cervical glands were enlarged and tender. Local treatment for the throat was applied, with no relief of symptoms.

The patient, admitted July 2 at 3:50 a. m., complained of vomiting, fever and sore throat of thirty-six hours' duration. The family history was essentially irrelevant. She had had measles, chickenpox, German measles and whooping cough in childhood. There had been no other previous illnesses or hospital admissions. The systems were normal except for the pronounced obesity since childhood. The menses had not yet begun. There was no history of allergic reactions. The present illness began on the morning of June 30, when the patient began to vomit apparently after a dietary indiscretion, the vomitus at first being partly digested food and later containing bile; the temperature was 101 F., which began to rise progressively to 105.6 F. The patient complained of pain in the throat and abdomen and of intense heat and thirst. At no time did the patient take aminopyrine or related drugs.

Examination.—On admission, the patient appeared acutely ill and was irrational. The face was flushed, circumoral pallor present and the skin hot and dry. The submaxillary glands

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Read before the Bronx Hospital Clinical Society, Oct. 8, 1934.

1. Dintenfass, Henry: An Ear Complication from Dinitrophenol Medication, J. A. M. A. **102**: 838 (March 17) 1934.
2. Jackson, Harry, and Duvall, A. I.: Dinitrophenol Poisoning: Report of a Case, J. A. M. A. **102**: 1844 (June 2) 1934.
3. Subsequent to the preparation of this paper there appeared in THE JOURNAL, Oct. 6, 1934, a report by Dr. Solomon Silver of a fatal case of agranulocytosis following dinitrophenol therapy with pneumonia complicating the terminal picture.
4. Hoffman, A. M.; Butt, E. M., and Hickey, N. G.: Neutropenia Following Amidopyrine, J. A. M. A. **102**: 1213 (April 14) 1934.
5. Bohn, S. S.: Agranulocytic Angina Following Ingestion of Dinitrophenol, J. A. M. A. **103**: 249 (July 28) 1934.
6. Davidson, Elizabeth N., and Shapiro, Matthew: Neutropenia Following Dinitrophenol, with Improvement After Pentnucleotide and Leukocyte Cream, J. A. M. A. **103**: 480 (Aug. 18) 1934.
7. Tainter, M. L., and Wood, D. A.: A Case of Fatal Dinitrophenol Poisoning, J. A. M. A. **102**: 1147 (April 7) 1934.
8. Geiger, J. C.: A Death from Alpha-Dinitrophenol Poisoning, J. A. M. A. **101**: 1333 (Oct. 21) 1933.
9. Masserman, J. H., and Goldsmith, Harry: Dinitrophenol, J. A. M. A. **102**: 523 (Feb. 17) 1934.
10. Tainter, M. L.; Stockton, A. B., and Cutting, W. C.: Use of Dinitrophenol in Obesity and Related Conditions, J. A. M. A. **101**: 1472 (Nov. 4) 1934.

were palpable and tender, and the throat was deeply injected, with purulent exudate present on the tonsils and uvula. The pupils were contracted, were equal and regular, and gave a normal reaction to light (there was no accommodation, since the patient was irrational and uncooperative). The thyroid was not palpable. The heart was normal except for a tachycardia. The lungs were normal. The blood pressure was 100 systolic and 68 diastolic. The abdomen was normal except for a moderate number of silvery striae in the lateral aspects of the lower part of the abdomen. There was slight pretibial edema, knee jerks and tendon reflexes were diminished but equal, and no abnormal reflexes were present. The temperature was 105.6 F., the pulse was 136 and synchronous with the heart beat, and respirations were 32.

Laboratory examinations[11] revealed the following: Blood count: hemoglobin, 88 per cent; red blood cells, 4,600,000; white blood cells, 700; lymphocytes, 100 per cent; platelets, 180,000. Blood chemistry: dextrose, 148.2; urea 16.2; nonprotein nitrogen, 35.3; uric acid, 3.2; creatinine, 1.23; cholesterol, 115.6; carbon dioxide combining power, 41.2 volumes per cent.

Examination of the urine showed the following: Specimen 1, July 1, was a dark amber and slightly cloudy. The Derrien test was positive for dinitrophenol.

Specimen 2, July 2, was a dark amber and slightly cloudy and had an acid reaction and a specific gravity of 1.019; albumin was 2 plus. It was negative for sugar, acetone, diacetic acid and urobilinogen; bile was present. There were very few fine and coarse granular casts, an occasional red blood cell and an occasional white blood cell. The Derrien test was negative for dinitrophenol.

Specimen 3, July 3, was orange, cloudy, acid, with a specific gravity of 1.017; albumin was 3 plus. It was negative for sugar, acetone and diacetic acid; bile was present. There were a few fine and coarsely granular casts, an occasional red blood cell and an occasional white blood cell. The Derrien test was negative for dinitrophenol.

Direct smear of the throat showed gram-positive cocci. Culture yielded Streptococcus viridans of the alpha type.

The diagnosis was dinitrophenol poisoning and secondary agranulocytic angina.

Course of Illness.—Before admission, the patient had been given a high colonic irrigation, salicylates and sodium bicarbonate, 20 grains (1.3 Gm.) of each, instilled in a rectal drip and followed by hydrotherapy. The vomiting ceased and the tongue appeared less dry. On admission the patient was given a saline hypodermoclysis, 5 per cent dextrose intravenously, and a rectal drip totaling 3 liters of fluids. One-fourth grain (0.016 Gm.) of morphine was administered, repeated and supplemented with 2 cc. of 50 per cent magnesium sulfate. Two cubic centimeters of liver extract was given intramuscularly and repeated intravenously. The delirium, restlessness and perspiration persisted. A blood transfusion of 400 cc. of whole blood was given ten hours after admission, which improved the patient's condition somewhat. Twelve hours after admission the patient began to show signs of laryngeal edema; the temperature was 105.4 F.; the pulse was 120, of feeble tension, poor quality and irregular; respirations were 24 and stertorous in type; the lips and nails were cyanotic, the uvula and pharynx were markedly edematous, necrotic and cyanotic in color; the heart sounds were of fair quality, rapid and occasionally irregular. The patient was placed in an oxygen tent. An ice cold rectal drip was instituted and an ice pack was applied. The patient was still incoherent and restless, exhibiting a marked tremor of the body and incontinence of stools. Sedatives in the form of bromides and a mixture of opium and alkaloids were ineffective and frequent alcohol sponges were given; the temperature was still elevated to 105.4 F. The pulse was 130, intermittent and of poor quality. The patient was cyanotic and gasping for breath in spite of oxygen administered nasally. Twenty hours after admission the patient was taken to the operating room in a moribund condition; she was cyanotic and unconscious; breathing was barely audible with marked stridor, and the accessory muscles of respiration were in use. To combat the laryngeal stenosis, direct laryngoscopy and bronchoscopy were attempted, but with failure, and tracheotomy was performed by Dr. Kleinfeld. At this point the patient's condition became much worse, and the bronchoscope was passed through the tracheotomy incision. The patient ceased breathing and failed to respond to artificial respiration, coramin and intracardiac epinephrine.

Autopsy.—The relevant postmortem observations were as follows:

External examination showed no ecchymosis or petechiae and moderate postmortem rigor, with no lividity present.

Subcutaneous fat was very pronounced. All abdominal organs appeared to be in normal position. The peritoneum was smooth and glistening.

The liver measured 27 by 16 cm. On section, the parenchyma showed advanced fatty changes.

The gallbladder was distended with about 20 cc. of greenish bile. No calculi were seen. The common, cystic and hepatic ducts were patent.

The pancreas measured 12 by 6 cm. No gross pathologic changes were noted.

The spleen measured 14 by 8 cm. The capsule was wrinkled. On section the pulp was friable and congested.

The stomach showed no gross pathologic changes.

In the small intestine there were numerous focal hemorrhagic necroses and some superficial ulceration in Peyer's patches and hyperplastic solitary acuminate lymph nodes.

No gross pathologic condition was noted in the large intestine.

Each kidney measured 19 by 9 cm. The capsules stripped easily. On section, no gross pathologic condition was noted.

Each adrenal measured 4 by 1 cm. and showed no gross pathologic changes.

No gross pathologic condition was present in the bladder. The ureters were patent.

The uterus was small and infantile.

The ovaries showed numerous follicle cysts at the periphery.

The heart showed no free fluid in the pericardial cavity. The heart measured 9 by 7 cm. The musculature of the left ventricle measured 13 mm. in thickness. No gross pathologic condition was seen in the myocardium, endocardium or pericardium.

Each lung measured 20 by 10 cm. and showed no gross abnormal changes.

No adenopathy was present.

The thyroid measured 4 by 4 cm. No gross pathologic condition was noted.

There was no evidence of fracture of the skull. The meninges did not show abnormal changes. No pathologic changes were noted with regard to the cranial nerves. The ventricles showed no evidence of hemorrhage. The cut surfaces of the cortex, medulla, cerebellum, pons and proximal portion of the spinal cord showed no evidences of inflammation or of pathologic changes.

Microscopic Examination.—In the liver there were extensive fatty changes in the center of the liver lobule about the central vein.

The spleen showed extensive vascular congestion; there were hyaline thrombi present in the sinusoids.

The kidney presented evidence of acute hemorrhagic nephritis. Many lymphoblastic plasma cells were noted in the congested vessels, and tubular hemorrhages were present.

The lungs showed no noteworthy pathologic changes except for vascular congestion.

A colloid goiter was present in the thyroid with early focal calcific deposits.

The ovaries showed congestion of the ovarian vessels.

The pituitary showed vascular congestion.

There was no depression evident of the bone marrow activity in a study of the vertebral bone marrow.

There were several superficial ulcerations of the mucosa of the intestine.

Culture of the heart's blood proved negative.

A postmortem blood specimen gave a positive Derrien reaction for dinitrophenol.

COMMENT

Agranulocytic angina of Friedemann, agranulocytosis of Schultz, malignant neutropenia of Schilling, pernicious leukopenia of Fitz-Hugh and Krumbhaar and granulopenia are interchangeable terms, all designating

11. We are indebted to Dr. Joseph Felsen, director of laboratories and research, for the hematologic, chemical, bacteriologic and postmortem studies reported in this paper.

not only an absence of neutrophils but also a marked decrease in all the granulocytes. Our patient's blood smear showed only 700 white blood corpuscles, the cells being entirely lymphocytes. Of all the possible etiologic factors such as bacterial infection,[12] an allergic basis,[13] congenital weakness of the bone marrow,[14] an endocrine disturbance,[15] special bone marrow selectivity, aminopyrine and the benzene ring compounds, of which dinitrophenol is a member, the specific history of ingestion of the drug pointed definitely toward dinitrophenol. The drug was recovered from the urine and from the postmortem specimen of the heart's blood as exhibited by positive Derrien tests. Furthermore, the symptomatology and the clinical course of the case followed regularly, step by step, definite mechanistic characteristics of a granulopenic process.[16] Pathologic study of the bone marrow showed no depression of bone marrow activity. The significance of this is of debatable interpretation in view of nine necropsies in cases of granulopenia reported by Fitz-Hugh and Comroe.[17] Our patient took the drug in subfebrile doses for a period of forty days. She could have readily taken 6½ grains (420 mg.) daily with presumably no untoward effects,[18] since her weight was 265 pounds (120 Kg.). But her daily dosage was 1½ grains (97.5 mg.). Apparently the only possibility of explanation here is in the effect of cumulative toxicity of prolonged administration. Since there is no known antidote, treatment was aimed at supportive measures for the maintenance of the life and the strength of the patient and at bone marrow stimulation. Because of the rapid, fulminating course of the case, supportive measures were relied on mostly.

SUMMARY

1. There have been only four cases reported to date of acute granulopenia following ingestion of dinitrophenol. In three of these cases recovery occurred; the fourth ended fatally.

2. In our case death occurred eighty-four hours after the onset of symptoms of poisoning following the ingestion of dinitrophenol in subfebrile doses over a period of forty days. Agranulocytic anginal symptoms presented themselves thirty-six hours after onset.

3. Autopsy failed to reveal any changes in the granulopoietic system.

4. The patient weighed approximately 120 Kg. Her daily dosage, according to the work of Cutting and his associates,[18] could have been 6½ grains with no untoward effects over a prolonged period of time. However, this girl took only 1½ grains daily over a period of forty days, during which time she lost 25 pounds. On the forty-sixth day the patient showed a marked febrile reaction.

5. The dosage in this case was low over a prolonged period and certainly within the presumed limits of safety. Hence this fatality can be attributed either to cumulative toxicity or to an idiosyncrasy to the drug.

6. At present there is no criterion by which to evaluate the sensitivity of a patient to the drug.

7. We have at our disposal, besides close supervision of the administration of the drug, the clinical measures of a check up of the daily temperatures and pulse rates, of blood counts, metabolic rates and weight loss.

8. There is no known specific antidote for dinitrophenol poisoning. The only remedy that seems to hold any promise, and which has been used efficaciously, is pentnucleotide. Unfortunately, because of the acute fulminating nature of the illness, it was not considered advisable to use pentnucleotide in our case. Other measures, such as oxygen, ice packs, alcohol sponges, iced proctoclyses, intravenous dextrose infusions and morphine, are essentially supportive in character.

Fulton Avenue at One Hundred and Sixty-Ninth Street.

12. Dennis, E. W.: J. Exper. Med. **57**: 993 (June) 1933.
13. Pepper, O. H. P.: The History of Agranulocytic Angina, J. A. M. A. **97**: 100 (Oct. 10) 1931.
14. Strumia, M. M.: Am. J. M. Sc. **187**: 826 (June) 1934. Wolff, E.: Folia haemat. **44**: 38 (April) 1931, quoted by Strumia. Burkens, J. C. J.: Nederl. tijdschr v. geneesk **75**: 2722 (May 23) 1931, quoted by Strumia.
15. Hubble, Douglas: Lancet **2**: 113 (July 15) 1933.
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17. Fitz-Hugh, Thomas, Jr., and Comroe, B. I.: Am. J. M. Sc. **185**: 552 (April) 1933.
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EFFECTIVE METHOD OF TREATING AMEBIC ABSCESS OF THE LIVER

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This paper is prompted by the fact that, in spite of definite and very marked lessening of the mortality rate in cases of amebic abscess of the liver treated by aspiration, the idea is little known in most parts of the country except those where amebiasis is common, the literature revealing that many of these patients are still subjected to surgery.

Rogers [1] in 1910 suggested the treatment of amebic abscesses by aspiration and reported several cases treated thus with good results. In 1920 Duckworth [2] mentioned treatment by aspiration and irrigation but did not report any cases. Ludlow [3] reported ten cases of amebic abscess treated by aspiration and emetine injections with no fatalities. Thurston [4] reported sixty-four cases treated with emetine and aspiration with a mortality rate of less than 25 per cent.

There are many advantages to treatment by this method over surgery. In the first place, by the time the diagnosis has been made the patients have suffered for some time with a chronic wasting disease and are poor surgical risks generally. In reported series of cases the surgical mortality has ranged well over 50 per cent. In the second place we are not dealing here with a true abscess; that is, there is no frank suppuration. The material obtained from the abscess consists only of necrotic liver tissue mixed with blood. In other words, if one can entirely evacuate the cavity and eradicate the cause there is little more we can hope to accomplish. Thirdly, these patients are usually ambulatory within a few days.

Contributing to the high surgical mortality is the fact that most of these cases with open drainage become secondarily infected, resulting in prolonged hospitalization, convalescence, and in many instances death.

DIAGNOSIS

A liver abscess should be suspected in every obscure case in which there is pain in the right upper quadrant of the abdomen with an enlarged and tender liver. Many of the abscesses rupture under the diaphragm, producing an elevation of the diaphragm with dulness,

From the St. Louis City Hospital.

1. Rogers, L.: Treatment of Amebic Abscess of the Liver, Indian M. Gaz. **45**: 493, 1910.
2. Duckworth, Sir Dyce: The Diagnosis and Treatment of Tropical Hepatic Abscess, J. Trop. Med. **23**: 149 (June) 1920.
3. Ludlow, A. I.: Treatment of Abscess of Liver by Aspiration and Subcutaneous Injections of Emetine, China M. J. **38**: 93 (Feb.) 1924.
4. Thurston, E. O.: Liver Abscess, Lancet **2**: 1008 (Nov. 15) 1924.

absent breath sounds and voice sounds in the right lower part of the chest. X-ray examination reveals the elevated diaphragm. There is usually a history of fever, malaise, and perhaps chills for several weeks or months. A history of diarrhea or dysentery is helpful, but absence of such a history by no means rules out an abscess. Patients with such symptoms and signs in absence of other explanation deserve a cautious exploratory aspiration.

The majority of amebic abscesses are in the right lobe of the liver, and in nearly every instance they are large solitary lesions. The site of election for aspiration is in the tenth intercostal space either posteriorly or in the midaxillary line. The area is infiltrated with procaine hydrochloride and a 3 inch needle is inserted directly in until the typical reddish brown "pus" is obtained. As a rule the abscesses are large (from 300 to 400 cc. or larger) and very little difficulty is encountered in locating them. Frequently, by the time the patient presents himself to the doctor, the abscess has "pointed," and definite point tenderness may be elicited somewhere around the lower part of the thorax. In such a case the aspiration should be done in this region. In order to substantiate the diagnosis, after withdrawal of several hundred cubic centimeters of pus it is wise to instil 20 cc. of opaque oil and from 200 to 300 cc. of air into the abscess. It can then be outlined very nicely when the patient is roentgenographed in various positions.

METHOD OF TREATMENT

Once the diagnosis has been established, the patient is bridged across two beds in such a position that the part of the abscess nearest the surface will be in the most dependent position. In other words, if the abscess has "pointed" in the tenth intercostal space in the midaxillary line, the patient is placed on his right side with this region over the space between the beds. A large gage needle is then inserted into the tenth intercostal space and just through the wall of the abscess. The point of this needle is then in the most dependent portion of the abscess and in position to evacuate the contents of the lesion entirely. This needle is connected to a Wangensteen suction apparatus. A second large needle is then inserted into the abscess at any other point and connected to an ordinary gravity flask containing 1 : 2,500 emetine solution. The circuit is opened and the entire contents of the abscess are flushed out. In such a manner one evacuation is deemed sufficient. Several hundred cubic centimeters of the emetine solution is left within the cavity.

Simultaneously, the patient is started on emetine hydrochloride according to the method suggested by Reed,[5] 1 grain (0.065 Gm.) of emetine hypodermically for six days followed by one-half grain (0.03 Gm.) for eight days, making a total course of 10 grains (0.65 Gm.). As brought out by Reed, emetine in larger doses may be quite toxic and this course of ten grains has proved to be sufficient. The response to such treatment is rapid. Within a few days the patient feels normal, is free from fever and is allowed up. The liver shrinks markedly and approaches normal size. The patient is allowed to go home and told to return every month for a check up and x-ray examination of the liver. Though the patient is symptom free, it requires several months for the abscess to disappear. Instead of giving the emetine hypodermically, Soper [6] has obtained excellent results by the use of emetine hydrochloride intravenously, giving 1 grain a day for seven days.

When the hepatic amebiasis has subsided, the patient should be given a thorough course of carbarsone to eliminate any remaining intestinal amebiasis. Arsenicals such as carbarsone and acetarsone are naturally contraindicated in hepatic amebiasis.

REPORT OF CASES

CASE 1.—E. J., a white man, aged 35, entered the hospital Nov. 25, 1935, complaining of gradual loss of weight and strength, malaise and fever, growing progressively worse for three months. He also complained of pain in the right shoulder for three weeks. He had several night sweats. On close questioning he stated that for five or six months he had had from four to five soft brown stools a day, without blood. His physician told him it was normal for some people to have this many stools. The history was essentially negative otherwise.

The patient was emaciated, with dulness, absent breath sounds and voice sounds in the right lower part of the chest. The blood pressure was 108 systolic, 60 diastolic. The liver was down four fingerbreadths below the costal margin and was moderately tender. The heart was regular without murmurs. The apex beat was in the fifth intercostal space in the nipple line. The temperature was 103, pulse 114, respiration 26. The urine was normal. Blood culture gave negative results. The Kahn reaction was negative. The blood sugar was 112 mg. per hundred cubic centimeters of blood; nonprotein nitrogen, 23 mg. Red blood cells numbered 4,904,000, white blood cells 20,400, with basophils, eosinophils and myelocytes 0 per cent, juveniles 4 per cent, stabkernige 33 per cent, segmented forms 44 per cent, lymphocytes 19 per cent, monocytes 0 per cent and hemoglobin 85 per cent.

Proctoscopic examination revealed from ten to fifteen shallow ulcers the size of match heads in the lower sigmoid. Some of the material from these ulcers was placed on a slide with warm saline solution and proved to be swarming with motile amebas containing red blood cells. X-ray examination of the chest revealed a density in the right base which was suggestive of an elevated diaphragm. A needle was inserted into the tenth intercostal space posteriorly and 750 cc. of dark brown "pus" aspirated. Twenty cc. of opaque oil was then instilled into the abscess and x-ray examination revealed this to be in the middle of the liver. The patient was treated by the method described. He became free from fever within a few days and has made an uneventful recovery, gaining 20 pounds (9 Kg.) within two months. The diminution in size of the abscess was followed by x-ray examination.

CASE 2.—J. H., a white man, aged 35, entered the hospital Jan. 21, 1936, complaining of a sharp pain in the right upper quadrant of two weeks' duration. He also stated that he had had an intermittent diarrhea of one month's duration, for which he had taken some medicine obtained from the drug store. The stools were watery with tenesmus, but there was no blood. On admission there was no diarrhea.

The patient was well nourished and appeared acutely ill. No definite abnormalities were apparent in the lung fields. The heart was regular, with no murmurs, and was not enlarged. The liver was four fingerbreadths below the costal margin and quite tender. In the tenth and eleventh intercostal spaces in the midaxillary line there was moderate fulness and definite point tenderness in the tenth intercostal space in the midaxillary line. The temperature was 100, pulse 88, respiration 32. The Kahn reaction was negative. Nonprotein nitrogen was 25 mg. per hundred cubic centimeters of blood, blood sugar 72 mg., amylase 12. Red blood cells numbered 3,000,000, white blood cells 16,900, basophils, eosinophils, myelocytes and juveniles, 0 per cent, stabkernige 18 per cent, lymphocytes 18 per cent, segmented forms 64 per cent, monocytes, 0 per cent, hemoglobin 75 per cent.

Proctoscopic examination revealed a normal mucosa in the sigmoid and rectum with no evidence of ulceration or bleeding.

In view of the observations, a needle was inserted into the tenth intercostal space at the region of point tenderness and the typical chocolate colored material of an amebic abscess obtained. Eight hundred cc. of the "pus" was aspirated and 500 cc. of air instilled along with 20 cc. of opaque oil to facil-

5. Reed, A. C.: Treatment of Amebiasis, J. A. M. A. **103**: 1224 (Oct. 20) 1934.
6. Soper, H. W.: Treatment of Amebic Dysentery, Am. J. Digest. Dis. & Nutrition., March, 1924.

itate x-ray studies. The stools were consistently negative for blood or amebas.

Two days later drainage and irrigation were performed in the manner described. Two days following this the temperature, pulse and respiration were normal and have remained so. The patient was out of bed in five days and made a rapid recovery, gaining 35 pounds (16 Kg.) in eight weeks.

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THE SUCCESSFUL TREATMENT OF ESSENTIAL THROMBOPENIA WITH HEMORRHAGE BY ROENTGEN RAYS

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Stephan,[1] only four years after Frank's [2] description and separation of thrombopenic purpura as a distinct entity, resorted to roentgen treatments over the spleen and reported cures of two "fulminating" cases with this method. From this time there have been numerous reports of single cases or small series by irradiation. While some of the reported results have been favorable,[3] there have been some reports, as of Pancoast and his co-workers,[4] that have failed to confirm Stephan's enthusiastic and completely satisfactory pioneer efforts. Because of this, irradiation of the spleen is not universally accepted as being worth while and in the last few years seems to have fallen into disuse. This is strikingly shown in the series of Jones and Tocantins.[5] In their series of fifty-three patients only one was treated with x-rays. Fowler [6] in a recent review of 160 cases casually mentions x-rays as follows: "The use of roentgen rays over the spleen has been found to be of only temporary value."

I have found that roentgen treatment to the spleen is so satisfactory that it is impossible for me to understand why it has not come to be considered as practically a specific therapeutic agent in primary or uncomplicated thrombopenia with hemorrhage.

The present generally accepted worth of roentgen treatment cannot be better summarized than in the following quotations. These excerpts are from three of the best and most widely used textbooks on general medicine and treatment:

> Irradiation of the spleen with roentgen rays has been advised in purpura haemorrhagica. It may be beneficial when appropriately given but rather often will be found ineffective.[7]
>
> Irradiation of the spleen with small doses of x-rays occasionally benefits a patient somewhat.[8]

In the third textbook,[9] roentgen treatment is completely ignored.

RESULTS IN THE PRESENT SERIES

My associates and I have successfully treated seven cases of purpuric and nonpurpuric thrombopenia with hemorrhage by irradiation of the spleen with x-rays. The eighth case, which was complicated with acute myeloid leukemia, terminated unfavorably.

COMMENT ON CASES

Patient 2 had a 500 cc. transfusion of whole blood with no effect before x-rays were resorted to.

Patient 3 had 20 cc. of antivenin with no effect, prior to irradiation, but five days later after the thrombopenia had disappeared and the bleeding had ceased the patient developed an anaphylactoid purpura (Henoch-Schönlein type) from the antivenin. This was easily controlled with epinephrine and ephedrine.

Case 5 has been reported in detail by de Saussure and Townsend.[10]

Patient 6 has had great improvement in general health following the use of thyro-ovarian medication.

Case 7 has not been included in the table. The patient was a white boy, aged 8 years, who continued to bleed from an incision for the removal of infected inguinal glands. A diagnosis of thrombopenia with hemorrhage with a platelet count of 25,000 was made. An additional diagnosis of acute myeloid leukemia was made forty-eight hours later. Following three roentgen treatments to the spleen the platelet count went up to 85,000 but the leukemia could not be controlled and the child died Dec. 13, 1934, six weeks after admission.

I believe, in spite of the smallness of the series, that uncomplicated thrombopenia with hemorrhage should be divided into two distinctly different classes; cases of unknown etiology (probably endocrine in origin), as cases 1, 6 and 8, and others from various toxemias,

Summary of Eight Cases in Which Roentgen Treatment Resulted in Complete Arrest of Thrombopenia

Case	Race	Sex	Age	Diagnosis	Manifestations	Platelet Count: Admission	Platelet Count: Dismissal	Follow Up	No. of X-Ray Treatments
1. E. Q.	White	♀	29	Purpuric thrombopenia	Bleeding from gastro-intestinal and genito-urinary tracts; purpurae	11/3/32 20,000	11/18/32 210,000	5/1/36 No return	6
2. J. M.	Negro	♂	30	Purpuric thrombopenia	Bleeding from gums and genito-urinary tract; petechiae	10/31/33 36,000	12/13/33 260,000	12/1/34 No return	1
3. M. K.	White	♀	23	Purpuric thrombopenia	Bleeding from all orifices and skin lesions	2/24/34 70,000	3/10/34 280,000	5/1/36 No return	2
4. M. H.	White	♀	7	Purpuric thrombopenia	Bleeding operative incision and ecchymoses	4/30/34 81,000	5/6/34 192,000	5/1/36 No return	3
5. M. B.	Negro	♀	35	Nonpurpuric thrombopenia	Bleeding from genito-urinary tract	5/11/34 33,000	6/16/34 237,000	1/17/36 No return	2
6. G. R.	White	♀	15	Nonpurpuric thrombopenia	Abnormal uterine bleeding; bleeding gums	7/13/34 80,000	8/3/34 187,000	5/1/36 No return	6
8. S. M.	White	♂	24	Nonpurpuric thrombopenia	Bleeding from gums and genito-urinary tract	3/3/36 20,000	4/15/36 290,000	6/7/36 No return	6

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The material for this brief is taken from a thesis submitted for membership to the American Roentgen Ray Society and has been released for publication in this manner rather than in its official journal, the American Journal of Roentgenology and Radium Therapy.

1. Stephan, R.: The Reticulo-Endothelial Cellular System of the Spleen in Relationship to Blood Coagulation, München. med. Wchnschr. **67:** 309 (March 12) 1920.
2. Frank, E.: Die essentielle Thrombopenie, Berl. klin. Wchnschr. **52:** 490-494, 1915.
3. Schreiner, B. F.: Radium and X-Ray Treatment of Myopathic and Thrombopenic Menorrhagia, Radiology **17:** 796-799 (Aug.) 1931.
4. Pancoast, H. K.; Pendergrass, E. P., and Fitz-Hugh, Thomas: The Present Status of the Roentgen-Ray Treatment of Purpura Haemorrhagica by Irradiation of the Spleen, Am. J. Roentgenol. **13:** 558-567 (June) 1925.
5. Jones, H. W., and Tocantins, L. M.: The Treatment of Purpura Haemorrhagica, J. A. M. A. **100:** 83 (Jan. 14) 1933.
6. Fowler, W. M.: Thrombopenic Purpura, Ann. Int. Med. **9:** 1475-1487 (May) 1936.
7. A Text-Book of Medicine, ed. 3, Philadelphia, W. B. Saunders Company, edited by Russell L. Cecil, the Section on the "Blood Forming Organs," edited by Minot and Buckman, p. 1048.
8. Beckman, Harry: Treatment in General Practice, ed. 2, Philadelphia, W. B. Saunders Company, 1934, p. 504.
9. Osler's Principles and Practice of Medicine, edited by Thomas McCrae, ed. 11, New York, D. Appleton & Co.
10. de Saussure, H. W., and Townsend, Eleanor W.: Purpura Haemorrhagica in Pregnancy, Am. J. Obst. & Gynec. **29:** 597-599 (April) 1935.

cases 2, 3, 4 and 5.[11] For convenience I have termed these respectively as cases with an excessive S factor (overdestruction of platelets by the spleen) and the others of C factor type (toxic destruction of platelets in the circulation). This division is important from the standpoint of radiation treatment. In the C factor type the spleen's normal function needs only to be lowered until the toxemia is overcome, and from one to three roentgen treatments will usually accomplish this. In the S factor type, unless the patient responds partially to other forms of therapy also it may be occasionally necessary to render the spleen permanently functionless by intensive irradiation.

TECHNIC OF THE TREATMENTS

The same technical factors were purposely used throughout this series. The generator is a one-half wave, valve rectified, 220 kilovolt peak capacity installation. The tube has been a thick glass, large bulb, open bowl, high voltage therapy apparatus of the Coolidge type. The following were used in all of the treatments: voltage, 200 kilovolt peak; tube current, 4 milliamperes; filter, 0.5 mm. of copper plus 1 mm. of aluminum; roentgens per treatment, 200 measured in air; roentgens per minute, 10; area exposed, anteriorly over the spleen; size of field, 20 cm. circular.

CONCLUSION

Roentgen radiation constitutes an exceedingly valuable and possibly a specific therapeutic agent when applied over the spleen in primary or uncomplicated thrombopenia with hemorrhage either with or without purpuric skin manifestations.

Clinical Notes, Suggestions and New Instruments

THROMBOCYTOPENIC PURPURA INDUCED BY PERTUSSIS TOXIN IN ALLERGIC CHILDREN

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Immunization against whooping cough is not without its dangers. They depend more on the constitution of the child than on the toxicity of the vaccine. Three allergic children developed thrombocytopenic purpura following the subcutaneous injections of B. pertussis vaccine obtained from different sources. The onset of the purpura came as a surprise without any premonitory signs by which the condition could be foretold. In one case purpura appeared within ten days, in the second during the second week and in the third case during the third week after the final injections. The purpura can be attributed to the activation of a preexisting but latent hemorrhagic state in one child. But in the two other children it is necessary to look for the pathologic lesion engendered by the pertussis toxin. And from the rarity of thrombocytopenic purpura as a complication in immunization it is apparently dependent on the allergic constitution.

The genesis of the purpuric state involves capillary toxicosis, megakaryocyte injury or both. There is ample clinical and experimental evidence that pertussis toxin is capable of inflicting such damage. B. pertussis forms no exotoxin, but an endotoxin is obtained from cultures which produces, experimentally, hemorrhagic lesions in animals. The contention that hemorrhagic manifestations observed in whooping cough are mechanical in origin is not substantiated by careful study. In an epidemic of whooping cough in an infantorium I observed hemorrhages in the conjunctiva, gums and lips, petechiae in the skin and blood in the urine and stool. The infants had ample antiscorbutic protection and no latent hemorrhagic disease prevailed. In fact, more hemorrhagic symptoms were observed when the coughing was least severe. In all specific fevers some form of purpura may be the complication. But following immunization against pertussis only localized subcutaneous hemorrhages appeared at the site of injection in many children and purpura was induced in the following three cases:

CASE 1.—S. S., an allergic girl aged 4 years, referred by Dr. Tully of New Castle, Ind., developed purpura within ten days of immunization against whooping cough in September 1935. Large ecchymoses suddenly appeared throughout the body assuming the characteristics of hemorrhagic hives. Oozing from the gums and petechiae of the mucous membranes occurred following ingestion of solid food. There was no epistaxis or blood in the urine or stool. The condition persisted for six weeks, with a slight elevation of temperature. No drugs were offered the child during the immunization, nor was the purpura preceded by any infection. Spontaneous recurrences of milder nature appeared in November and again in December 1935.

Physical examination during the last episode showed fine petechiae throughout, sparsely distributed. The mucous membranes were unaffected. The eyes were puffy, the nasal breathing obstructed, and there was a postnasal drip, cervical lymphadenitis, retro-auricular intertrigo and a positive tourniquet test. The spleen was not palpable, the liver not enlarged. The child was found sensitive to the toxin of pertussis and to that of the organisms obtained from the maxillary sinuses. The blood showed 81 per cent hemoglobin, 4,600,000 red blood cells, 11,200 white blood cells, 47 per cent polymorphonuclears, 29 per cent lymphocytes, 12 per cent staff cells, of which 8 per cent were eosinophils, and 129,000 platelets, a rise from 88,000. The clotting time was five minutes, the bleeding time five minutes. The blood group was II. Transfusion was performed, the patient was maintained on a nonallergic diet, and the sinuses were treated. The child has remained free from purpura to date.

CASE 2.—T. M., an allergic child aged 2 years, referred by Dr. Lathrop of Plainfield, N. J., developed an exacerbation of purpura within the third week of immunization against whooping cough in July 1935. Confluent purpuric spots appeared over the lower extremities, with no other hemorrhagic manifestations. The blood showed a mild secondary anemia, platelets 85,000, bleeding time seventeen minutes, clotting time five minutes, clot retraction delayed. The tourniquet test was positive. There was no evidence of infectious invasion. The spleen was palpable at the costal border. The condition promptly abated with a transfusion, intramuscular blood and a clotting dietary.

The child had recovered from the first attack of purpura ten months previous to the immunization against whooping cough. At 5 months of age the gums over the erupting first incisors appeared hemorrhagic. Transient purpuric eruptions developed over increasing areas of the lower extremities. The physical examinations gave negative results. The blood picture was characteristic, with 34,000 platelets; the bleeding time was thirty minutes, clot retraction was markedly delayed, and the tourniquet test was positive. With a nonallergic clotting regimen and a transfusion the child recovered, the platelets having risen to 600,000.

CASE 3.—A. C., an allergic girl aged 5 years, referred by Dr. Sarkany of Long Island, developed purpura during the second week of the final immunizing dose of whooping cough vaccine in April 1936. Large ecchymoses appeared over the face and left arm and later similar patches, firm, raised and plum colored, covered the eyes, wrists and backs of the hands. There was occasional but slight epistaxis and hematuria and some elevation of temperature but no disturbance in the child's demeanor. The bleeding time, clotting time, blood count and platelet content were essentially normal. The condition gradually abated, when within a fortnight a paroxysmal cough developed which aggravated the purpura.

Physical examination showed waxy pallor and subconjunctival and cutaneous hemorrhages. A symmetrical dark purpuric

11. The toxic factors were, in order, case 2, acute specific urethritis and rheumatic fever; case 3 followed German measles; case 4 was associated with pyogenic cervical adenitis, and in case 5 there was a toxemia of pregnancy.

area covered the cheeks and nose. There were small petechiae over the trunk and limbs but none involving the mucous membranes. The ecchymoses were adjacent to bony prominences and pressure points with slight trauma apparently localizing the bleeding. The temperature was high, the pulse was rapid, the respirations were shallow. The pharynx was injected and the cervical lymph glands were enlarged. There were coarse mucous râles throughout the chest. The spleen was not palpable and the liver not enlarged. The reflexes were normal. Early one morning the child became restless, screamed and was found semiconscious. The head was retracted, breathing was stertorous, the movements of the extremities were involuntary. There was also involuntary micturition and defecation. There were all the evidences of a complete right-sided hemiplegia, an upper motor neuron lesion spreading to the left side and finally involving the whole body. With embarrassment of the vital centers she died five hours after the onset of the cerebral hemorrhage that morning.

1060 Park Avenue.

THE USE OF CARBON TETRACHLORIDE IN THE REMOVAL OF ADHESIVE TAPE

REPORT OF A NEAR FATAL CASE

FREMONT A. CHANDLER, M.D., CHICAGO

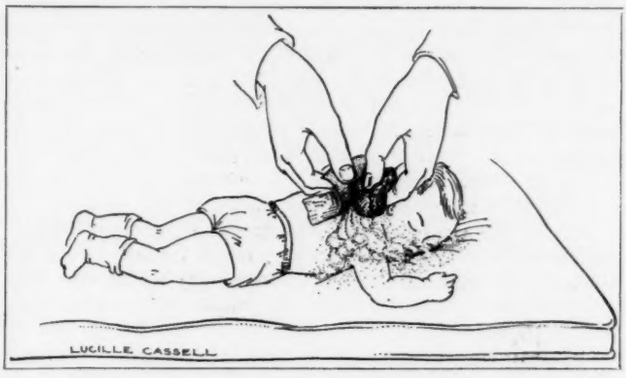
In view of the aroused interest in adhesive solvents since the recent tragic accident in a midwestern university training camp in which two lives were lost, there is danger of exchanging fire hazards for less familiar, asphyxiative ones. Benzine or similar products are inflammable and must be protected from open flames or sparks. These products are more efficient in the removal of adhesive tape and of desquamated epithelium. They are well tolerated by young patients. The potential danger of fire is probably only slightly greater than that present in the use of alcohol solutions which are on every dressing tray or cart.

On the other hand, carbon tetrachloride softens desquamating skin only slightly. Its odor is offensive to children who have had recent anesthetics.

Carbon tetrachloride and similar chemicals have definite and dangerous anesthetic properties. A recent issue of *Time* describes the use of carbon tetrachloride as a means of killing foxes so as not to injure their pelts. The vapor is heavy, a feature enhancing its use as a fire extinguisher. Its use by some otolaryngologists in irrigating the external auditory meatus is to be condemned because of the possibility of leakage into the pharynx by way of the eustachian tube.[1]

The following case is reported to show that the free circulation of air in a large, open ward is not sufficient to eliminate the anesthetic properties of carbon tetrachloride under certain conditions:

C. P., a white girl, aged 4 years, had tuberculous spondylitis of the third and fourth and the seventh and eighth dorsal vertebrae of eighteen months' duration. A spine fusion operation to immobilize the diseased area of the spine was performed without any shocking effect on the patient. Convalescence was highly satisfactory. Solid food was tolerated within twelve hours. The operative dressings, which were held in place by adhesive tape, were changed on the fourth day by the intern. While he was removing the dressings, the child was prone. Carbon tetrachloride, which had been substituted for benzine by the hospital authorities because of the potential fire hazard, was used as a solvent to facilitate the removal of the dressings (see illustration). The patient collapsed suddenly, respirations ceased and the radial pulse became impalpable. Death appeared imminent. Artificial respiration was instituted. In about five minutes the pulse returned, as did active respiration, at first feebly, and then stronger. In about ten minutes the child was quite normal. The subsequent convalescence has been uneventful.



Method of removing adhesive tape from the back, showing spread of heavy asphyxiating vapor of carbon tetrachloride.

This case is reported as a warning against the indiscriminate use of carbon tetrachloride in the removal of dressings from the upper part of the body, head and neck.

The presentation of carbon tetrachloride solutions and allied substances as safe solvents for the removal of adhesive tape under certain circumstances must be questioned. The layman is probably more familiar with the dangers of inflammatory mixtures than with those of heavy vapors possessing toxic potentialities.

6 North Michigan Avenue.

1. The following references relative to the toxicity of carbon tetrachloride have been published within the last two years:

Desoille, H., and Antoine, G.: Intoxication par un mélange de tétrachlorure de carbone et d'essence de pétrole destiné au nettoyage des cheveux (Intoxication from Mixture of Carbon Tetrachloride and Benzine Used for Shampoo), Ann. de méd. lég. **16**: 155-157 (March) 1936.

Gonzaes, T. A.: Fatal Inhalation of Dry Cleaning Fluid, J. A. M. A. **106**: 286 (Jan. 25) 1936.

Lehnherr, E. R.: Acute Carbon Tetrachloride Poisoning: Report of a Case, Arch. Int. Med. **56**: 98-104 (July) 1935.

Tomb, J. W., and Helmy, M. M.: Toxicity of Carbon Tetrachloride and Its Allied Halogen Compounds, J. Trop. Med. **36**: 265 (Sept. 15) 1933.

Carbon Tetrachloride in Industry, editorial, J. A. M. A. **107**: 590 (Aug. 22) 1936.

Smyth, H. F.; Smyth, H. F., Jr., and Carpenter, C. P.: The Chronic Toxicity of Carbon Tetrachloride: Animal Exposures and Field Studies, J. Indust. Hyg. **18**: 277 (May) 1936; abstr. J. A. M. A. **107**: 461 (Aug. 8) 1936.

Dervillee, P.: L'intoxication experimentale par le tétrachlorure de carbone; données générales et récherches personnelles (Experimental Carbon Tetrachloride Intoxication: General Considerations and Personal Research), J. de méd. de Bordeaux **113**: 91-102 (Feb. 10) 1936.

Davis, P. A.: Carbon Tetrachloride as an Industrial Hazard, J. A. M. A. **103**: 962-966 (Sept. 29) 1934.

Löwy, J.: Die chronische Vergiftung mit Tetrachlorkohlenstoff (Chronic Poisoning with Carbon Tetrachloride), Arch. f. Gewerbepath. u. Gewerbehyg. **6**: 157-159, 1935.

AMEBIASIS AND PSEUDOPOLYPOSIS OF THE COLON

HAMILTON H. ANDERSON, M.D.; DANIEL DELPRAT, M.D.; ALANSON WEEKS, M.D., AND ALFRED C. REED, M.D.
SAN FRANCISCO

Although polyposis of the colon is not uncommon and malignant transformation is known to occur,[1] the etiology of polyps is still a matter of conjecture. In fact, we seem no closer to the solution of this problem than Wagner[2] was in 1832 when he "described the formation during the healing process of pedunculated polypoid, little warts on the margins of the ulcers and on certain smooth patches on their surface." He evidently did not suspect, however, that the warts were really folds of the diseased mucous membrane itself.[3] Irregular, polypoid masses of mucosa are often found at the margins of ulcers in the process of healing or are formed by the undermining of part of the mucosa in cases of chronic dysentery and chronic ulcerative colitis. Woodward[3] terms this pathologic entity "pseudopolyposis of the colon," thus distinguishing it from the colonic tumors of idiopathic origin referred to by Virchow. Since Woodward's description in 1881, many efforts to classify polyps of the colon have ended in confusing rather than clarifying the picture of this disease. Today it is recognized, however, that two general types of polyposis occur; namely, the condition first described by Wagner[2] and the diffuse adenoma-

1. Lawrence, J. C.: Gastro-Intestinal Polyps: Statistical Study of Malignancy Incidence, Am. J. Surg. **31**: 499 (March) 1936.
2. Wagner, J., quoted by Woodward.[3]
3. Woodward, J. J.: Am. J. M. Sc. **81**: 142, 1881.

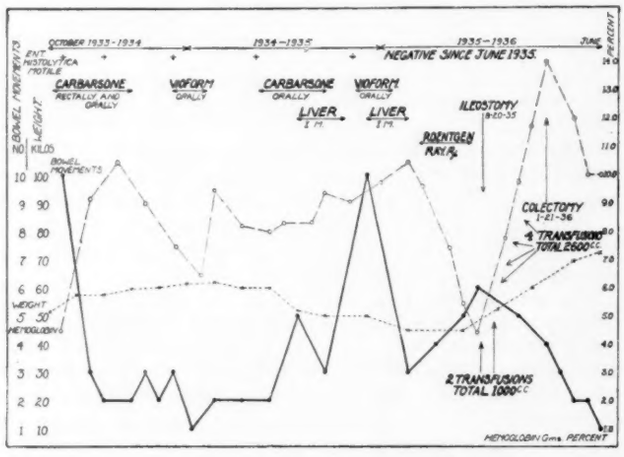
tosis of Cripps.[4] Wesson and Bargen[5] indicate that inflammatory mucosal tags or pseudopolyps follow such diseases as chronic ulcerative colitis, tuberculosis or severe amebiasis. Ten per cent of 1,600 cases of chronic ulcerative colitis reviewed by them presented inflammatory polyps as a sequel and 25 per cent of these might develop carcinoma, according to their statistics.

The following case is presented as one of pseudopolyposis of the colon occurring in a person with chronic, severe amebiasis and chronic ulcerative colitis:

REPORT OF CASE

J. O'N., an Irish nursemaid, aged 30, was seen first on Oct. 24, 1933, when she complained of "tropical dysentery." On arriving from Ireland eight years before she had severe dysentery, with bloody, mucoid liquid movements and complained of fever for a five months period. A physician demonstrated amebas in her stools one year after onset and she was given nine injections of emetine, which afforded her temporary symptomatic relief. During the next five years she had four recurrences of dysentery with fever, at which times she was treated expectantly with temporary improvement of her status.

In 1931 she was given nine treatments of emetine hypodermically and 100 pills of chiniofon, which caused nausea and vomiting but gave relief from the dysentery for a time. One



Clinical course during thirty months.

year later she had nine more injections of emetine, which were followed by dyspnea, palpitation and increased heart rate after exercise, and weakness. The intestinal symptoms cleared until two months before we saw her, since when she has had from fifteen to sixteen liquid, bloody, mucoid movements daily with cramps, but no nausea, vomiting or fever. Four months before, her hemoglobin was 28 per cent. The family history was unimportant. Ten years before, the right lobe of her thyroid was removed. Her habits were regular. Her average weight was 125 pounds (57 Kg.) but at the examination she weighed 115 pounds (52 Kg.), the loss occurring during the past four months.

On examination she was afebrile and pale, with a slightly subicteric tint to the mucous membranes and skin. The left lobe of the thyroid was fuller than the right. The area of cardiac dulness was increased to the left and the heart sounds were of fair quality, with a systolic murmur at the apical and aortic areas. The pulse was regular, with a rate of 90. The blood pressure was 112 mm. of mercury systolic, 60 diastolic. The abdomen was distended with palpable masses in both lower quadrants and was tender in the sigmoid area. The liver edge was felt at the costal margin.

Laboratory tests revealed 1,940,000 red cells, hemoglobin 28 per cent (Sahli), 4.4 Gm. per hundred cubic centimeters, and 8,760 white cells, with 67 per cent neutrophils, 20 per cent lymphocytes, 8 per cent eosinophils, 3 per cent monocytes and 2 per cent megalocytic neutrophils. The urine was normal. Endamoeba histolytica (motile) was demonstrated in the stool in smears stained with iron hematoxylin. Culture of the stool was negative for bacilli of the typhoid-dysentery group. Blood agglutinations were negative. The basal metabolic rate was minus 12 per cent. An electrocardiographic tracing[6] showed a rate of 93, slight SA tachycardia, a PR interval of 0.24 second, latent partial auriculoventricular block, and an abnormal lead 4, suggesting cardiac abnormality.

Our diagnosis at this time was:

1. Amebiasis, with colitis, dysentery and secondary anemia.
2. Myocardial damage, due to excessive emetine therapy.

Her progress during the thirty-three months that she has been under our care is outlined in the accompanying chart. The patient harbored Endamoeba histolytica for the first eight months of this period, but thereafter no amebas were seen on repeated examination of the stools. Thirty grams of carbarsone was given orally and 10 Gm. instilled rectally, and 30 Gm. of vioform was administered. In addition, soluble iron salts were prescribed throughout and a smooth diet high in protein. Solution liver extract-Lilly was given on two occasions intramuscularly, 100 cc. in divided amounts each time. Roentgen examination was delayed until June 24, 1935, because of the patient's financial status. When severe dysentery recurred, however, and the patient lost 20 pounds (9 Kg.) in three months without exhibiting amebas in her stools, other causes of her symptoms were searched for. Sigmoidoscopic examinations from the beginning showed an ulceration of the lower bowel which was characteristic for chronic amebiasis but which failed to clear under specific therapy. Roentgen examination of the bowel by means of a barium sulfate enema[7] revealed marked spasticity of the entire colon with multiple polypi, most marked in the descending and transverse colon. Since the patient was a very poor operative risk and refused surgical care, we resorted to roentgen treatment as a palliative measure. She had a total of 1,100 roentgens from June 25 to July 29, 1935, but became so weakened by the increasing dysentery and decreasing hemoglobin (it fell to the original level of 4.4 Gm. per hundred cubic centimeters) that she finally consented to an exploratory laparotomy. Two transfusions of 500 cc. were given before operation, which increased the hemoglobin from 7.8 Gm. per hundred cubic centimeters and red cells 2,140,000, to hemoglobin 9.0 Gm. and red cells 3,700,000. The white count was 5,200 cells, with 73 per cent neutrophils and 5 per cent eosinophils.

Operation was performed Aug. 20, 1935, from 10:45 to 11:22 a. m., by Dr. Weeks. Nitrous oxide and ether anesthesia was used. A low left paramedian incision was made through the skin and a very small amount of subcutaneous tissue. The abdomen was opened without difficulty. The colon was immediately visualized and palpated. At about 5 cm. distal to the ileocecal valve the intestine was contracted and hard. The serosa was granular and wrinkled and had lost entirely its customary sheen. On palpation the colon appeared hard, rubbery and firm, calling to mind the feel of a much used garden hose. This condition obtained throughout the entire colon to the rectum, only the head of the cecum appearing normal. On account of the extensive involvement of the entire colon, ileosigmoidostomy was not possible as had been planned, and accordingly a loop of ileum was brought out through a stab wound in the right flank and sutured to the abdominal wall. The abdomen was closed in the usual manner. The patient absorbed 1,500 cc. of saline solution subcutaneously during the operation.

After this preliminary operation the patient was allowed to convalesce for about five months, during which time she was at rest in bed. She received frequent 500 cc. transfusions during this time. Dilute solutions of potassium permanganate or acriflavine hydrochloride were employed in washing out the lower part of the bowel. The patient showed marked clinical improvement but failed to gain weight. Since we had roentgen evidence of polyposis of the bowel and since we believed that malignant change might occur[8] in the polypoid masses, we

4. Cripps, W. N.: Tr. Path. Soc. London **33**: 165, 1882.
5. Wesson, H. R., and Bargen, J. A.: Proc. Staff Meet., Mayo Clin. **9**: 789 (Dec. 26) 1934.
6. By Dr. John J. Sampson.
7. By Drs. I. S. Ingber, F. H. Rodenbaugh and R. F. Kile.
8. Reed, A. C., and Anderson, H. H.: Am. J. M. Sc. **191**: 237 (Feb.) 1936.

strongly advised complete colectomy. She finally agreed to undergo this rather formidable operation, which proved to be a life-saving procedure.

The operation was performed Jan. 21, 1936, from 8:43 to 10:25 a. m., by Dr. Delprat. A long left rectus incision was made through the previous operative scar. The abdomen was opened without difficulty. There were no adhesions to the abdominal wall from the operation in August. The entire colon was palpated and found to have remained exactly as noted at the previous operation. The colon however appeared movable and not bound down, so that colectomy appeared feasible. Accordingly the cecum was drawn toward the wound and the distal loop of the previous ileostomy was divided and closed. The lateral attachments of the ascending and descending colon were divided, allowing excellent mobility. The omentum was separated from the anterior surface of the transverse colon, following which the entire colon was removed down to the sigmoid, the mesentery being ligated. This procedure was accomplished without difficulty, but in separating the lower rectum from the sacrum a large perforation was produced through the abnormal intestine and considerable soiling of the peritoneum followed. The intestine therefore was merely loosened as far down as possible and then cut across with scissors. The peritoneum was closed over it as in the method of Coffey, with intraperitoneal and extraperitoneal drainage. The patient was then placed on her side and the remainder of the rectum and anus removed from below, the cavity being packed with gauze soaked with potassium permanganate solution. Following the operation, while the patient was still on the table, she was given 500 cc. of whole blood.

Pathologic examination of the entire colon by Dr. W. P. Stowe showed reddened, hemorrhagic areas, with discrete ulcerations and multiple areas of polypoid excrescences of granulation tissue, none of which exceeded a centimeter in height or width. Microscopic sections showed lymphoid hyperplasia in the mucosal and submucosal coats, increased numbers of eosinophils, plasma cells, and round cells with some polynuclear cells between and beneath the glands. In some sections, islands of round cells and eosinophils were seen extending into the muscularis zone. The glands showed no evidence of malignant change, but superficial ulceration and necrosis were seen frequently in the crests and in the cryptlike folds of mucosa. Polypoid outgrowths of the adenomatous type were not seen.

Several ulcerated areas of the colon were sectioned and the tissue was stained with iron hematoxylin and searched carefully for amebas, but none were demonstrated.[9]

For fourteen days following the operation the patient's temperature did not exceed 37.5 C. (99.5 F.). Her pulse varied, however, from 120 to 140 for sixteen days, thereafter gradually returning to normal. This might be expected because of the soiling at operation. The entire abdominal wound became infected and broke open to the peritoneum. Secondary suture was not possible because of the adjacent discharge ileostomy, so that approximation of the wound edges with adhesive plaster seemed advisable, although unsatisfactory on account of the patient's abdomen being scaphoid at all times. Under treatment with gentian violet solution, however, the wound gradually filled in and was entirely healed on her discharge from the hospital on April 4, 1936.

Since leaving the hospital the patient has gained rapidly in strength, weight and hemoglobin level. When last seen (July 22, six months after colectomy) she was symptom free, her abdominal wound was entirely healed, she averaged two evacuations daily, her weight was 54 Kg. and her hemoglobin was 13.6 Gm. per hundred cubic centimeters, with 4,270,000 red cells and 8,240 white cells, with a normal differential count.

SUMMARY

Pseudopolyposis of the colon occurred in a patient successfully treated for amebiasis but unsuccessfully treated for coexisting chronic ulcerative colitis. Colectomy proved a life-saving measure in spite of the patient's extreme debilitation, emetine poisoning and anemia due to eight years of chronic, severe dysentery.

350 Post Street—St. Luke's Hospital.

9. Courtesy of Dr. Herbert Johnstone.

Special Article

THE PHARMACOPEIA AND THE PHYSICIAN

THE USE OF ANTISYPHILITIC REMEDIES

H. N. COLE, M.D.
CLEVELAND

This is one of a series of articles written by eminent clinicians for the purpose of extending information concerning the official medicines. The twenty-four articles in this series have been planned and developed through the cooperation of the U. S. Pharmacopeial Committee of Revision and THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.—ED.

In syphilis there is an active, motile organism which requires moisture and tissue for its further spread and vitality. It is well known that Spirochaeta pallida dies within one-half hour if exposed on a dry surface; e. g., a glass slide. On the other hand, if anywhere on the body the organism gains entrance into the skin, through a bruise, a cut or a crack, an infection will probably occur. Of this there is not absolute surety, for it is possible that certain individuals may have some resistance to the disease, perhaps enough at least to ward off an isolated contact. If the organism does penetrate the skin and multiply, the spread is probably quite rapid. One can remember the time when it was considered good therapy to excise the chancre. Now it is felt that there is extension to the draining lymph nodes within a few hours, and probably some of the spirochetes are to be found in the heart blood within a matter of a day or a few days at the most. The multiplying organisms at the site of penetration of the skin finally set up an immune reaction on the part of the host consisting of an infiltrate of serum of mononuclear elements and of fibroblasts; this is spoken of as the chancre or the primary lesion.

The multiplying organisms spreading through the draining lymph chains set up a characteristic, sharply defined, indurated, painless, enlarged type of node with satellite, smaller nodes around it. The syphilitic nodes do not fuse together. They are quite movable and, unless secondarily infected, do not break down. Through the lymph channels and blood stream there is an early further spread of the infection to other parts of the body, notable to the ectodermal elements, resulting in an eventual further immune reaction on the part of the host anywhere from eight to twelve weeks after the infection, known as the secondary stage or eruption. It appears first on mucous membranes and shortly thereafter on the skin. It is also found on the walls of the bladder, on the viscous surfaces and on the meninges. The eruption may be profuse or sparse. There is still difference of opinion as to the amount of relationship between the amount of eruption and the intensity of the disease. There is also recognized the so-called symptomless infection in which the primary lesion and the secondary changes may have been absent or so evanescent that the first intimation the patient may have of an old syphilis may be a positive blood Wassermann reaction, a tabes dorsalis, an aneurysm or a mysterious devastating ulceration of the skin. Sooner

From the Department of Dermatology and Syphilology, Western Reserve University School of Medicine.

or later, the secondary manifestations of the disease gradually disappear as the result of treatment or as the result of an increasing amount of immune bodies being built on the part of the host. With occasional later flare-ups the disease gradually drifts into a further stage of latency, in which physical examination may reveal no symptoms of the syphilis and it can be diagnosed only by the history and by a serologic examination. This period of dangerous silence may last for years. It is the period of time in which organisms deposited in the lymph nodes and in the tissues cause chronic fibrotic changes with endarteritis, which may eventually result in a frank aortitis, in a meningo-arteritis, in a hepatitis, or in a gumma of the skin or bone. For some of these changes there may be an exciting cause—trauma. For aortitis, race may play a part; e. g., the Negro. For some there may be no explanation. It is certain that the central nervous system process, e. g., tabes or dementia paralytica, or the insidious aortitis, are laid down early in the course of the disease by deposition of the organism in the vasa vasorum. The central nervous system syphilis is not a change developing "out of the blue" ten or fifteen years after the infection. The syphilitic person who has had little or no treatment may well have developed a basilar meningitis secondary to an infection of the vasa vasorum or thereby the beginnings of a later tabes or dementia paralytica may have been laid down. Moreover, the aortic insufficiency or the aneurysm is an early rather than a late concomitant of an untreated or poorly treated syphilitic disease, allowing specific changes to take place in the vasa vasorum which eventually cause weakening of the vessel walls, scar formation and retraction of the aortic leaflets.

PUBLIC HEALTH RESPONSIBILITY IN SYPHILIS

Given a case of syphilis in its early stages, there is a heavy public health responsibility on the part of the physician. All contacts in the home should be repeatedly checked, especially in case the patient is married. Moreover, even in this day and age it may be necessary to examine conditions in the patient's place of business. I was recently consulted by a man with a chancre of the lip and was amazed to find that a common drinking cup was being used in his manufacturing plant, where several hundred men were at work. In all cases of early syphilis, all contacts should be carefully checked by the physician. It may mean the prevention of numerous transfers of the disease to innocent persons. With a preventable disease such as syphilis the medical profession does not exercise sufficient care in diagnosing the disease, in picking it out in its daily work and in properly handling its various manifestations. How many physicians bother about routine Wassermann tests on their patients? And yet many puzzling complaints or signs will be revealed by this single act. It is true that around 30 per cent of all syphilis is latent in character—to be recovered only by careful questioning and positive serologic reactions. And yet it is this 30 per cent of patients who may, in part, be the spreaders of new infections through relapses or act as transfer agents of the disease to the next generation through pregnancy. Moreover, a certain number of them may even then be developing an aortitis or a dementia paralytica. From 25 to 30 per cent of the inmates in asylums are suffering from syphilis, poorly treated or never treated. The Cooperative Clinical Group,[1] in a recent study of cardiovascular syphilis, found that 69 per cent of the patients had never had any treatment for syphilis. This should indicate to physicians the necessity of more careful examinations of the patients, including routine Wassermann tests. When syphilis is discovered, its thorough treatment is paramount. The medical man is surely in the Court of Public Opinion with regard to this situation, and if it is not properly met the state will next step in and assume full responsibility for handling this disease.

RESULTS DERIVED FROM ANTISYPHILITIC DRUGS

In considering a drug worthy of trial in the treatment of syphilis, several criteria are to be considered:

1. The drug should be cheap enough to be available to all.

2. It should be in as simple a form as is possible, not requiring a too elaborate technic for its administration. Because of this criticism our most potent antisyphilitic remedy, arsphenamine, is rarely employed outside syphilis clinics and hospitals. Neoarsphenamine is more easily administered.

3. The remedy should be free from attendant unpleasant symptoms, such as pain, nausea, emesis and headache. Moreover, severe systemic after-effects should not follow its use.

4. Its action should be relatively rapid in alleviating acute symptoms of syphilis; thus, a remedy requiring more than a few days to destroy the spirochetes on moist papules on the lips is not sufficiently potent.

5. The summan bonum in the antisyphilitic drug is the preparation that at one dose will destroy all the organisms of the disease in the body without attendant harm to the host. This was Ehrlich's idea when he announced his six hundred and sixth trial compound. Unfortunately, it failed to satisfy the requirement. So we are now forced to rely on the drugs that will come closest to this desired result without too severe reaction to the host. Experience has shown that the three heavy metals in their proper salts—arsenic, bismuth and mercury—best answer these fulfilments. The efficiency of the respective metallic salts has been worked out through studying the rapidity of the disappearance of Spirochaeta pallida from inoculation chancres of rabbit testes.

Investigations have also been made on the rapidity of disappearance of trypanosomes from infected mice and rats. With the arsenicals this trypanocidal activity corresponds quite well with the treponemicidal rate, but unfortunately with bismuth compounds this is not the case.

As a definite ratio of the effect of a drug against the spirochetes, one employs what is known as the therapeutic ratio—the maximal tolerated dose over the minimal effective dose. From microscopic study of the rapidity of disappearance of spirochetes after heavy metal therapy from inoculation chancres in rabbit testicles, and through transplants to further rabbit testes of the infected testicular material it has been possible to work out the therapeutic ratio. Thus, arsphenamine has a ratio of from 20:1 to 30:1.

It is true that the mistake must not be made of too closely comparing rabbit syphilis to human syphilis. It is well known that rabbit syphilis may actually be eradicated from the host; with the human variety this is certainly not such an easy proposition. The chemotherapeutic ratio for potent bismuth preparations runs around 50:1 or more when the drug is used intramuscularly. Bismuth is ten times as toxic if used intra-

1. Cole, H. N., Usilton, Lida J., and others: Deliberations Eleventh International Dermatological Congress, Budapest, Patria, 1935, p. 430.

venously and should never be employed by that route. With mercury the chemotherapeutic ratio is only 1:1 or 1:2. Thus it is easily understood why the trend of syphilis therapy has been more and more to arsenical and bismuth salts.

ACTION OF THE HEAVY METALS IN SYPHILIS

It is hardly the scope of this short article to consider the mode of action of the heavy metals against syphilis. This has been taken up at length in various publications both here and abroad. It is known that a mercury salt rubbed into a chancre swarming with spirochetes causes them to disappear. Yet the dosage of mercury in vitro sufficiently large to destroy the organisms, if used in life, would kill the host as well. It is probable with all three of these metals that the action is, in part, a specific one but also has some effect on the body cells that enables them, in turn, to overwhelm the spirochetes. Probably the arsphenamines when injected are transformed in the body into a more potent form, arsenoxide, before they exercise their effect, and Levaditi thinks that the bismuth salts are activated by extracts of the tissues into a much more active compound, which he terms "bismoxyl."

PREFERRED MODE OF ATTACK IN TREATING SYPHILIS

The elder Fournier was considered to be one of the greatest syphilologists of his time, and no doubt he did much to spread knowledge of syphilis. Moreover, he was one of the earliest adherents to the theory that tabes dorsalis was due to syphilis. This was long before any specific organism had been discovered.

However, the intermittent treatment for syphilis that he so strenuously practiced and advocated undoubtedly impeded the advance of syphilis therapy for many years. In fact, even today, as a result of his teaching, some very able men still employ an intermittent mode of attack in handling this disease. Fournier went on the theory that the physician using mercury was employing a potent remedy, toxic to the liver, bones and gastro-intestinal tract, but especially so to the kidneys. Therefore the patient undergoing treatment should take mercurials for a time, alternating these courses with purposeful rest periods. Such a form of treatment was kept up for from three to four years, the length of the rest periods being gradually increased and the courses of treatment being decreased. It is true that Fournier did not have the additional more potent heavy metals bismuth and arsenic to aid him in his work.

It is to the credit of Almkvist in Europe and almost simultaneously to the credit of Keidel and Moore in this country that attention was called to the disadvantages of the intermittent treatment of syphilis. If it were possible to give syphilitic patients large enough doses of arsphenamine and other heavy metals to cure them in one course of treatment there probably would be no schema necessary in treating syphilis. However, it must be realized that in syphilis one is dealing with a chronic infection due to an organism that, with our present remedies, disappears only gradually from the lymph nodes, skin and deeper structures. In fact, some men, like the late Dr. Warthin, claimed that they never entirely disappear; rather, that the disease is merely "arrested." At any rate, it is quite evident that in a situation comparable to this it would theoretically be unwise to treat the patient by an intermittent form of therapy. Grant that the organisms were checked by the arsenicals, the bismuth or even the mercury, would it not then stand to reason, if purposeful rest periods were instituted in the course of treatment, that during these periods, with the effect of the remedies removed, any viable organisms would once more start multiplying? Not only does this theoretically sound tangible, but in actual practice the writings of Moore and of the Cooperative Clinical Group would indicate its actual probability. And a recent report by Stokes of the League of Nations investigations comparing the results of the Cooperative Clinical Group, using the continuous system of treatment of syphilis as against the intermittent form of treatment employed by some of the large European clinics, revealed a very favorable comparison for continuous treatment.

Instead of giving the patient purposeful rest periods after a course of arsphenamine or preparations of bismuth or mercury, the treatment is alternated. Perhaps the patient with an early syphilis receives a course of arsenical injections, which is followed at once by a course of intramuscular injections of a bismuth compound. This in turn is followed by another course of arsenical treatment. In this manner, by alternating the drugs, one keeps the disease under continuous attacks with some form or other of antisyphilitic therapy.

Moreover, there is another very important argument in favor of continuous treatment; viz, the problem of relapse in syphilis. In the Cooperative Clinical Group Studies,[2] it was found that relapses as a rule came early in the course of syphilis. In the group material 25 per cent came in the first six months after infection, and by the end of the second year 85 per cent of the relapses to occur had intervened. The average time of relapse was eighteen months after infection and it occurred as a rule nine months after the last treatment. In other words, a physician treating an early case of syphilis should follow the patient carefully during the first two years of the disease, as this is the critical period for relapse to appear. This has been the bugaboo not only of the family physician but also of the syphilologist in treating syphilis. The patient with an early syphilis has been put on antisyphilitic therapy, has done nicely for a time, and all at once, on returning from his purposeful vacation period, is found to have a relapse of his Wassermann test to positive; or, again, he has returned with severe headaches, a lumbar puncture is done and he is found to be suffering from syphilitic meningitis. Perhaps he returns with a type of lesion even more dangerous to the public and to his family—the infectious relapse, in the form of a moist papule on his lip or with condylomata lata of the genitalia or rectum. The Cooperative Clinical Group found that relapses of all kinds, including Wassermann fastness, were much lower if continuous therapy had been employed, 13 per cent as against 21 per cent with intermittent therapy. Moreover, if irregular, haphazard treatment was used, the percentage of relapses mounted to 45. Finally, if the intensive form of therapy was employed, consisting of three or four daily maximal doses of arsphenamine followed by a series of heavy metal injections and purposeful rest periods, the percentage of relapses again was high, 41.

That intermittent treatment, with its vacation periods, is bad can be seen from still another angle. The Wassermann reaction in the earliest stage of the syphilitic chancre, up to ten or twenty or more days, is not

2. Stokes, J. H., and others: Compt. rend. des. séances, VIII Congress internat. de dermat. et de syph., Copenhagen, 1930, p. 768.

revealed in the syphilitic patient's blood. This is known in syphilologic parlance as the seronegative phase of the disease. It is the most favorable time in which to institute therapy, diagnosis being made on the primary lesion by means of the darkfield illuminator or by study of smears made from the serum of the chancre and appropriately stained with Wright's, Giemsa's or Fontana's stains. As sufficient reacting bodies to the disease are built up in the blood stream, the Wassermann reaction changes from negative to positive. Ordinarily this takes place at from fifteen to thirty days after the inception of the infection, depending on various circumstances. This stage of the disease is spoken of as the seropositive stage and really is little different from the secondary stage of syphilis. Without therapy this positive reaction on the blood remains for some years, after which a negative Wassermann reaction may gradually develop in a certain number of cases. Certain phases of late syphilis are more prone to a positive Wassermann than others; e. g., dementia paralytica, in which one encounters around 90 per cent of positive reactions. With tabes, and especially with Charcot's joints, on the other hand, the percentage of negative reactions may reach as high as from 30 to 40. It is unfortunately true that the Wassermann reaction is the "sine qua non" to all too many physicians and that as long as the Wassermann reaction is positive treatment is indicated. While this is many times a mistake, yet a persistently positive reaction with no reversal to negative in the experience of the Cooperative Clinical Group was seen much more frequently when intermittent treatment was employed. In fact, with continuous therapy there was reversal of the reaction to negative in 82 per cent of the cases, as contrasted with but 37 per cent in which intermittent treatment with purposeful rest periods was employed. And with aimless, irregular treatment such as the patient all too often takes into his own hands there were but 5 per cent of Wassermann reversals. Undoubtedly most of the persisting positive blood Wassermann reactions in early syphilis can be laid at the door of purposeful rest periods in the course of treatment, thus allowing the spirochetes in the body to start multiplying once more and build up new foci of disease. The general waging a vigorous campaign against the enemy allows no respite, no breathing spells. The same policy should apply when the physician takes on himself the great responsibility of handling a case of early syphilis. If the victory is not won in the first two years, it is going to be a long campaign. Undoubtedly the rest periods offer opportunity for the laying down on syphilitic cardiovascular disease of central nervous system involvement and the like.

The amount of treatment administered also has a great bearing on the factor of relapse. In the Cooperative Clinical Group material, of those patients receiving twenty or more arsenical treatments with interim heavy metal, only 12 per cent had an infectious relapse, while, on the other hand, 64 per cent of the patients receiving but one to four injections of an arsenical with interim heavy metal had relapsed, while if even five to nine were given, but one-seventh as many patients relapsed. And in connection with syphilis of the central nervous system three times as many neurorecurrences developed if less than twenty injections of an arsenical with interim heavy metal were employed as when more than twenty were employed. Indeed from a study of relapses seen in the group material it was possible to draw the deduction that adequate treatment of at least twenty to thirty injections of an arsenical and interim heavy metal in a case of early syphilis gave best promise of the patient's immune powers being supported and not broken down.

SYSTEMIC REACTIONS FROM ANTISYPHILITIC DRUGS

Before discussing the suggested outlines of treatment for various phases of syphilis, it may be well to devote a few words to systemic reactions observed from the drugs used. This is all the more important if one endeavors to follow more or less of a routine, especially in early syphilis.

Mercury is used less and less today, so that it is only necessary to recommend careful supervision of the kidneys in all patients taking mercurial preparations. Gastro-intestinal reactions in the form of diarrhea or bloody diarrhea, the patient himself will note. Fortunately the severe cases of mercurial stomatitis, even with ulceration, are rarely seen today.

With both bismuth compounds and arsenicals the kidneys are not so liable to be affected. Nevertheless, it is good practice with any patient under heavy metal therapy to examine the urine for albumin and red cells at every visit.

The patient undergoing treatment with heavy metals should be questioned at each visit as to any unforeseen happening following the last treatment. Gastro-intestinal reactions, itching of the skin, sores in the mouth, headaches, blurring of vision, may all be very significant. The gastro-intestinal reactions are usually the result of the arsenicals. If they persist with succeeding injections, despite abstinence from meals, it may require change of remedy. Occasionally the use of a tablet of Atropine Sulfate $\frac{1}{100}$ grain (0.0006 Gm.) one-half hour before the injection may obviate the reaction. Or if the patient develops a nitritoid reaction at the time of the administration of the arsenical, an intramuscular injection of Epinephrine, from 0.3 to 0.5 cc. of a 1:1,000 solution, will be of great value. Itching of the skin or any cutaneous reaction following bismuth, but especially arsenical therapy, should be the signal for careful check up of the causation. The best treatment of heavy metal reactions in syphilis therapy is prophylaxis. Telltale bluish lines on the gums are seen after bismuth, and one may even observe ulcerations in advanced cases. Severe headaches and puzzling "grip-like" attacks are occasionally seen after bismuth injections, though they are rarely recognized. Blurring of vision may be encountered after tryparsamide therapy of central nervous system syphilis. No patient should receive this drug until his visual and color fields have been carefully checked. Contracted fields are probably a contraindication to this form of therapy and any patient complaining of visual disturbances following tryparsamide should, for the time, have the treatment discontinued. With severe cutaneous reactions from the arsenicals the use of emollient measures rather than of stimulating remedies will be most helpful; e. g.

Rose Water Ointment

	Gm. or Cc.
℞ Rose Water Ointment	100.0

Misce. Signa: Apply locally as required.

Emollient

	Gm. or Cc.
℞ Boric Acid	5.0
Petrolatum	
Wool Fat	āā ad 100.0
Oil of Lavender	q. s.

Misce. Signa: Apply locally as required.

Some patients prefer plain Olive Oil in such a situation. Sometimes, when there is pruritus, the lotion given below will be found of value, the mercury being added to obviate folliculitis.

Lotion of Phenylmercuric Nitrate and Tannic Acid

		Gm. or Cc.
℞	Phenyl Mercuric Nitrate	0.018
	Glycerite of Tannic Acid	45.0
	Hamamelis Water ad	180.0

Misce. Signa: Apply locally as required.

Certain patients with a generalized infected dermatitis exfoliativa will get much relief from the use of hot potassium permanganate baths in a dilution of 1:5,000.

Many times, in patients suffering from the foregoing chronic condition, the use of Solution of Liver, either by mouth in doses of one teaspoonful, three times a day in orange juice, or of intramuscular injections of Purified Solution of Liver, 2 cc. every two or three days, may be very helpful in starting a turn for the better.

Rarely, fortunately, does the physician encounter an arsenical hemorrhagic encephalitis. It generally comes after but two or three injections and is initiated with high fever, headache, muscular twitchings and convulsions. Lumbar puncture should be performed at once to relieve pressure, and venesection may be of value. Here again intravenous injections of Sodium Thiosulfate 15 grains (1 Gm.) should be given once or twice a day for a few days if the patient survives that long. I have seen a patient already unconscious and having convulsions from this condition return to consciousness following a slow subcutaneous hypodermoclysis of 5 per cent dextrose, 500 cc. It may be repeated in three hours.

Hemorrhagic reactions following the use of the heavy metals should be the signal for their instant and probably permanent discontinuance. These reactions seem to be more frequent after the use of sulfarsphenamine, so much so that many syphilologists have discontinued its use. Blood dyscrasias have been seen after both bismuth compounds and arsenicals, and a routine white blood count, differential and platelet count should probably be done on every patient undergoing antisyphilitic therapy every two months, and in hospital practice this should be feasible every month.

With a granulocytopenia the first indication may be an acute deep ulceration in the throat. Transfusion is indicated, and pentnucleotide-N. N. R. may be tried, a 10 cc. vial injected intragluteally twice a day until the white blood cell count has definitely risen and thereafter once a day until the count has been normal for at least three days. Sodium Thiosulfate should also be used in 1 Gm. doses intramuscularly every day along with the same remedy by mouth in like doses of keratin coated capsules three times a day.

The appearance of icterus in the course of arsenical therapy is most disturbing. While syphilitic hepatitis is rare, it may occur, especially in an irregularly treated patient, or in a patient given purposeful rest periods. At times it is difficult to distinguish between a catarrhal icterus and an arsenical type. Probably all patients with icterus should have arsenicals discontinued for the time being, and if an arsenical process is finally diagnosed the patient should be treated with bismuth and mercury compounds in the future. Diet, elimination and Sodium Thiosulfate is indicated in such cases. Hypodermoclysis of 5 per cent dextrose solution may be of value. While not entirely convinced, I would recommend in a severe case the trial of decholin sodium N. N. R. intravenously, 5 or 10 cc. of the 20 per cent solution. A second and third injection of 10 cc. may be given on the succeeding two days, followed by decholin by mouth, from 0.25 to 0.5 Gm. (4 to 8 grains), two or three times a day after meals for several weeks.

The physician treating the syphilitic patient should be constantly on the lookout for unusual or unforeseen symptoms. These should be signals to discontinue treatment until the causation is explained. There is nothing more inexcusable than to see a severe generalized exfoliating dermatitis in a case in which the physician has given another dose of an arsenical after the telltale eruption has already appeared. Prophylaxis, prevention, is the watchword in using heavy metals for syphilis.

TREATMENT OF SERONEGATIVE AND SEROPOSITIVE AND SECONDARY SYPHILIS

It should be understood that in attempting an outline of treatment for early syphilis that there are bound to be exceptions. Such an outline is given with the hope of furnishing an ideal for treatment in terms of present day knowledge. Many times it cannot be carried out. Perhaps the patient is susceptible to arsenical therapy, or it may be that he develops symptoms of kidney irritation after the use of the other heavy metals, or again he may be one of those individuals who develop severe headaches after the use of bismuth compounds. There are bound to be such exceptions to the routine of treatment.

Again, the problem of type of arsenical to be used must be considered. Undoubtedly arsphenamine is somewhat more potent than neoarsphenamine, but it is questionable that the average physician in office practice will use the former because of its greater potency. It requires more manipulation: it also requires the use of normal sodium hydroxide, 0.85 cc. for each 0.1 Gm. of the drug. This is not always available and if in stock may be deteriorated. Consequently the average physician prefers neoarsphenamine. It is kept preferably in the icebox in the dark. The desired dosage is best sprinkled over the surface of from 8 to 10 cc. of sterile distilled cold water and then dissolved by gentle rotation of the container. The dosage is injected very slowly intravenously by means of a 10 cc. glass syringe. The injection should last at least one minute. There are far fewer reactions where the drug is injected slowly. In hospital practice and in well equipped large offices arsphenamine may be preferred, as sufficient drug for several patients may be prepared at one time. The drug is administered by the gravity method in a dilution of from 10 to 20 cc. of water for each 0.1 Gm. The intravenous injection should be delivered slowly. Stokes has called attention to "rubber tubing" reactions.

Another arsenical being employed quite extensively, and accepted by the Council on Pharmacy and Chemistry, is Mapharsen. It is administered by the intravenous route and is notable for the freedom from reactions, outside of gastro-intestinal reactions, following its use. It is employed in dosages of from 0.03 to 0.06 Gm., and the drug, after being dissolved in from 5 to 10 cc. of distilled water, is administered rapidly intravenously. If the dose is given slowly, the patient may complain of pain up the arm. In this respect, rapidity of administration, it differs from arsphenamines. Mapharsen has now been used quite extensively and seems to have found a place in the therapy of syphilis. It may be used in place of arsphenamine or

neoarsphenamine as the arsenical, especially if there is any reason why the others cannot be employed.

There are many bismuth preparations on the market, and many of them are quite efficient. It probably would be well for the physician to learn the action of but a few, well tried ones and depend on them. If a slower, but comparatively constant bismuth action is desired, one may use a suspension in oil of bismuth subsalicylate 0.13 Gm. (2 grains) intramuscularly in the buttock once a week for a course of from eight to twelve weeks, depending on circumstances.

Again, if it is desirable to get a more rapid bismuth action, one may employ one of the soluble preparations. Naturally, they will be absorbed and excreted more rapidly; hence it will require their administration two or three times a week. Such a type of therapy would be indicated more in hospital practice and perhaps when the patient is arsenic sensitive, forcing the physician to depend on preparations of bismuth and mercury to treat the disease. As intramuscular injection of Thiobismol 0.2 Gm. (3 grains) three times a week, of Iodobismitol 2 cc., or of the aqueous solution, bismuth sodium tartrate, 0.03 Gm. (one-half grain) two or three times a week would be indicated. Such therapy can be continued for a series of from fifteen to eighteen injections, depending on how the patient reacts.

REQUIRED TREATMENT FOR A CASE OF EARLY SYPHILIS

Given an average routine case of early syphilis, treatment should be kept up in a continuous form with alternating courses of arsenicals and preparations of bismuth or perhaps of mercury for at least one year after all signs and symptoms of the disease have disappeared. Thus the Cooperative Clinical Group [3] has found, from a study of several thousand cases of early syphilis, that anywhere from twenty to thirty, and preferably thirty, injections of arsphenamine and approximately the same number of insoluble bismuth injections or, under certain conditions, of mercury are necessary to give a satisfactory result. Neither drug should be used in less amounts, provided the patient stands them well. Too little of the arsenical or, again, too little of the bismuth may lead to resistant Wassermann-fast cases and to various types of relapse. In beginning the treatment of an early case of syphilis it is justifiable to shorten the intervals between the first three injections of the arsenical. This is done with the hope of getting the disease more rapidly under control. Moreover, with the last injection of each course of arsphenamine it is well to give the first injection of bismuth subsalicylate; thereby there is no interval of time in which the patient is not under continuous treatment. A Wassermann test of the blood should be made at the beginning and at the end of each course of treatment. Moreover, it is well to take a second Wassermann test the first and fifth days after the first arsenical injection of succeeding courses of treatment—the provocative Wassermann reaction. Often a negative reaction may be achieved by the end of the first or second course of treatment. It is desirable to hold this status, for treatment must be kept up for one year after all signs and symptoms have disappeared. A lumbar puncture should be done early in the course of the disease; otherwise a central nervous system involvement may be submerged temporarily by treatment. If it is negative, another should be performed before the therapy is discontinued at the end of eighteen months or two years. If, under continuous therapy, there is a return to a positive Wassermann reaction on the blood, early cardiovascular or central nervous system involvement should be ruled out. It must be remembered that an occasional patient will relapse no matter what is done for him; fortunately these cases are not common.

A careful routine physical examination should be made of the patient on starting therapy and repeated at least once a year thereafter. Moreover, after treatment is discontinued there should be a careful neurologic examination and fluoroscopic examination of the cardiovascular stripe. For several years after therapy is discontinued the patient should have a Wassermann test every six months and thereafter once a year, along with the routine physical examination that every individual should receive.

Solution of Potassium or Sodium Iodide

	Gm. or Cc.
℞ Potassium or sodium iodide.....	
Distilled Water .....āā	100.0

Misce. Signa: 10 to 20 drops in water after meals.

The place of potassium iodide or sodium iodide in the treatment of syphilis is still debatable. There is no question of its value in late syphilis and where it is desired to achieve a breaking down of the connective tissue barriers of syphilomas. The drug is of value in syphilitic meningitis in even larger doses and it should probably be prescribed with the courses of heavy metals even in early syphilis.

For purposes of convenience, a chart modified from the Cooperative Clinical Group Studies [4] is appended. It is noted that the therapy for seropositive primary and secondary syphilis is somewhat longer than for seronegative primary disease. The bismuth employed should be of a type that will furnish from 0.080 to 0.12 mg. of metallic bismuth at a weekly injection; thus it limits itself to either a liposoluble preparation or to an oil suspension if but a single weekly injection is employed.

LATENT SYPHILIS

One of the most important phases of syphilis is the so-called latent syphilis. It is that period in which it is impossible to make a diagnosis of the disease except through a clear cut history and a positive blood Wassermann reaction; in fact, many times even the history is not obtainable. A case showing spinal fluid changes but no pathologic condition on physical examination would be classed not as latent syphilis but as symptomless syphilis of the central nervous system. These latent cases are important, as in this period a submerged syphilis may be silently preparing the way for more active symptoms; e. g., of the aorta or of the central nervous system. Moreover, they may be important from a public health aspect through danger of infectious relapse or, in the female, transmissal to the next generation through pregnancy. Probably 30 per cent of all syphilis is in the latent stage and demonstrates too well the urgent routine use of the Wassermann test on all new patients consulting the physician. With latent syphilis, as Moore [5] well puts it, "the aim of treatment is no longer radical but instead clinical arrest and the prevention of infection to others." Thus the outline already given may be modified slightly to con-

3. Stokes, J. H.; Cole, H. N.; Moore, J. E.; O'Leary, P. A.; Wile, U. J.; Parran, Thomas, Jr.; Vonderlehr, R. A., and Usilton, Lida J.: Standard Treatment Procedure in Early Syphilis, J. A. M. A. **102**: 1267 (April 21) 1934.

4. Veneral Disease Information **10**: 2 (Feb.) 1929.

5. Moore, J. E., and others: The Treatment of Latent Syphilis, Ven. Dis. Inform. **13**: 317 (Aug.) 351 (Sept.), 371 (Oct.), 389 (Nov.), 407 (Dec.) 1932, **14**: 1 (Jan.) 1933.

sist of ten weekly injections of neoarsphenamine followed by ten weekly injections of bismuth subsalicylate, each 0.2 Gm., the foregoing being alternately used up to a total of thirty injections of each. Sodium or potassium iodide is indicated the first year along with the heavy metal courses and in the second year between the courses of heavy metals.

In the second year three ten injection series of bismuth salicylate may be given, a rest period of ten weeks being allowed between the injections. Daily inunctions of Strong Mercurial Ointment 4 Gm. may be employed in place of the bismuth subsalicylate during the second year, from fifty to sixty rubs being considered a course of treatment.

The necessity of continuous therapy is not so urgent after the first year of the disease, as the patient's own immunity is probably built up to a certain extent. Following the period of treatment, whether the blood Wassermann reaction is positive or negative, it would be well to follow the patient yearly with complete physical examination and laboratory check up. This is the type of patient who all too often, because of a positive blood Wassermann reaction and nothing else, is treated on and on ad infinitum.

This type of treatment may be suitable for late tertiary syphilis of the skin and bones, provided there is no involvement of the cardiovascular system. Potassium or sodium iodide is indicated at once in all later stages of syphilis for the purpose of absorbing connective tissue walls around syphilitic foci. In such a case it might be well even to continue the heavy metal therapy with rest intervals over a further period of one year.

CARDIOVASCULAR SYPHILIS

The medical profession is now beginning to realize that cardiovascular syphilis is one of the commonest and severest complications of late syphilis. Moreover, a recent survey by the Cooperative Clinical Group has shown that 62 per cent of the patients with uncomplicated syphilitic aortitis, 76 per cent of those with aortic regurgitation and 84 per cent of the group aortitis with sacculated aneurysm had been previously untreated for their syphilis. On the other hand, in a series of cases followed from three to twenty years, none of the patients developed aortic regurgitation or aneurysm provided they had been adequately and regularly treated during the early stages of syphilis. It is thus evident that the best treatment of cardiovascular syphilis is prophylactic, thorough, continuous treatment of the early disease. On the other hand, once the disease is established, much will depend on the condition found. Bed rest may be necessary for a time, and in the presence of cardiac breakdown pulverized digitalis 0.1 Gm. is indicated. Patients with edema may also be benefited by the diuretic action of the heavy metal salts; e. g., bismuth sodium tartrate 0.03 Gm., iodobismitol 2 cc., thiobismol 0.2 Gm. or mercuric succinimide 0.015 Gm., injected intragluteally three times a week. Certain patients will be unable to stand any arsenical and the physician must depend on preparations of mercury, bismuth and the iodides. Some patients, however, are much benefited by their cautious use. After a preliminary course of either mercury or bismuth compounds to prevent therapeutic shock, the patient may be started very cautiously on neoarsphenamine 0.05 to 0.1 Gm., gradually increased to a maximum dose of from 0.2 to 0.45 Gm. given to a maximum of ten to twelve weekly doses. Better results are achieved with smaller doses. In all cases, reactions of any type must be prevented in order to relieve strain on an already overburdened myocardium. Between succeeding courses of neoarsphenamine, courses of insoluble bismuth oil suspensions may be employed, e. g., bismuth subsalicylate, with good response. Alternating courses of the aforementioned drugs may be kept up for at least two years. Vigorous treatment must be avoided at all costs, and, naturally, every patient with cardiovascular syphilis should be kept under close observation, treated according to symptomatology, and, if possible, given a certain amount of treatment throughout life.

Schema of Treatment for Early Syphilis

Day or Week	Neoarsphenamine, Gm.	Interim Treatment	Blood Wassermann Test	Comment
Day				
1	0.3 to 0.45		1	Arsphenamine may be used, maximum 0.3 Gm. female to 0.4 Gm. male; mapharsen may be used in maximum 0.04 Gm. female to 0.06 Gm. male; spirochetes disappear from lesions in 24 to 48 hours; Wassermann reaction often negative by end of first course; do a lumbar puncture in this course of treatment; the first bismuth is given with the last arsenical injection
5	0.45 to 0.6			
10	0.45 to 0.6			
Weeks				
3	0.6			
4	0.6			
5	0.6			
6	0.6			
7	0.6			
8	0.6			
9	0.6			
10	0.6	Bismuth salicylate 0.2 Gm., 6 doses, 1 each week	1	
11				
12				
13				
14				
15				
16	0.6		1	Wassermann tests first day and fifth day after first arsenical
17	0.6			
18	0.6			
19	0.6			
20	0.6			
21	0.6			
22	0.6			
23	0.6			
24	0.6			
25	0.6	Bismuth salicylate 0.2 Gm., 8 doses, 1 each week	1	
26 to 33				
34	0.6		1	Provocative Wassermann
35	0.6			
36	0.6			
37	0.6			
38	0.6			
39	0.6			
40	0.6			
41	0.6			
42	0.6			
43	0.6			
44 to 54		Bismuth salicylate 0.2 Gm., 10 injections, 1 a week	1	Patients with seronegative primary syphilis cease treatment if Wassermann always negative, after this course of bismuth; provocative Wassermann
55	0.6		1	
56	0.6			
57	0.6			
58	0.6			
59	0.6			
60	0.6			
61	0.6			
62	0.6			
63	0.6			
64	0.6		1	
65 to 74		Bismuth salicylate 0.2 Gm., 10 injections, 1 a week	1	Seropositive primary and secondary syphilis, if all signs and symptoms negative 1 year, may be put on probation
75 to 123		No treatment		Blood Wassermann every month or two
123		Complete check up; physical examination; lumbar puncture; fluoroscopic examination of cardiovascular stripe; if both lumbar punctures are negative, no repetition required; physical examination every year and Wassermann, for a few years, every six months, and thereafter along with physical examination		

SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

The scope of this article will not allow anything more than a cursory review of which is considered good treatment for syphilis of the central nervous system. With early involvement of the central nervous system, a schema of treatment such as that suggested for early syphilis may be adopted, with the deletion of the first three doses of the arsenical in a space of ten days, the

doses being given once a week. Moore believes in the use of full doses of 0.75 Gm. of neoarsphenamine or 0.5 Gm. of arsphenamine in these cases. The treatment should be continuous, with alternating courses of arsenicals and preparations of bismuth. In case the process is of a vascular type or of a meningitic character, it may be well to hospitalize the patient and give a preliminary course of soluble heavy metal injections; e. g., iodobismitol 2 cc. or bismuth sodium tartrate 2 cc. twice a week for from eighteen to twenty-four injections, or of thiobismol 2 cc. three times a week for the same number of treatments. Naturally, potassium iodide or sodium iodide is indicated in such cases. Some men believe in the use of large doses; whether more will be achieved from enormous doses than from 1 to 3 Gm. three times a day is a question. In all syphilis of the central nervous system the effect of specific therapy should first be tried. Moreover, one is dealing with a disease due to an organism that is best met with such specific measures. The progress of the disease can be reviewed by the Wassermann reaction at the end of each course of treatment and by the lumbar puncture done every six months up to three or four times a year. More and more however the consensus is turning to the use of nonspecific therapy in all resistant syphilis of the central nervous system. Consequently, if after a year of treatment there has not been much response, a course of preferably malaria is to be recommended. In a recent comparison by Epstein, Solomon and Kopp [6] of malaria and diathermy in the treatment of dementia paralytica they found malaria to be preferable. If the patient can stand the treatment, a course of from ten to twelve or fifteen chills should be given. Following this treatment I prefer a course of neoarsphenamine, eight injections, each of 0.75 Gm., as soon as the patient is in a condition to stand it. This is given with the idea of attacking any surviving organisms that can be reached with specific measures. Then following a short course of bismuth injections the patient should be given a long course of tryparsamide, starting with an intravenous injection of from 0.5 to 1 Gm. and gradually working up to a maximum weekly dose of 2.5 Gm. As a preliminary to the treatment, the eyes should be carefully examined, as to both visual and color fields. If they are within the range of normal (not contracted) limits, the patient will probably have no reaction from this drug. Nevertheless, the physician should keep in mind the danger of damage to the optic nerve. Generally the symptoms show up within two or three weeks, with blurring and feathering of vision. In such a case treatment should be stopped for a week or more and later cautiously resumed. Often the therapy is continued up to a total of forty or fifty injections.

The patient with syphilis of the central nervous system is a problem in himself. It is difficult more than to outline the measures to be tried in such cases. A fair proportion will respond to the technic described; many will be resistant. On the other hand, there comes to mind a vascular central nervous system syphilis in a man aged 50, seen fifteen years ago, who never had anything except courses of injections of mercuric salicylate 0.09 Gm. intragluteally every week, or of bismuth subsalicylate 0.2 Gm., and potassium iodide by mouth. He is now clinically and serologically cured and his spinal fluid is entirely normal. At times the disease may respond quite satisfactorily; more often it will test the skill and knowledge of the physician at every turn.

6. Epstein, S. H.; Solomon, H. C., and Kopp, Israel: Dementia Paralytica, J. A. M. A. **106**: 1527 (May 2) 1936.

SYPHILIS AND PREGNANCY

Moore [7] has made the statement that an untreated syphilitic woman has only one chance in six of bearing a living healthy child as compared with three chances in four with a healthy woman. And this ignores the further fact that in children born alive of syphilitic mothers both the mortality and the morbidity rates are much higher than among the children born of nonsyphilitic mothers. However, prenatal syphilis is absolutely a preventable disease. It depends on frequent blood Wassermann tests throughout every woman's pregnancy and an immediate institution of specific therapy when the syphilis is discovered. Every pregnant woman should have a Wassermann test early in pregnancy, before the fifth month and again at the seventh or eighth month. The Cooperative Clinical Group [8] has found that far better results are achieved if the disease is discovered and therapy started before the fifth month of pregnancy giving preferably at least fifteen injections of arsphenamine or neoarsphenamine, and a like amount of appropriate heavy metal; e. g., bismuth salicylate. If syphilis is discovered late in the pregnancy, some treatment begun even at this time and continued up to the termination of pregnancy may be of great value in the production of a living child. If the pregnant syphilitic woman is seen early enough it may be possible to give a course of arsphenamine or neoarsphenamine or Mapharsen followed later by a course of bismuth. It is always well to terminate the therapy with an arsenical preparation because of its more potent action on the spirochetes. The woman who has had syphilis should probably be treated through every pregnancy because of danger of transmission of organisms to the fetus through the placental circulation. In isolated instances in which a patient is arsenic sensitive it would be well to give alternate courses of bismuth injections and of inunctions of Strong Mercurial Ointment up to the termination of the pregnancy, from forty to fifty rubs being considered as a course of treatment. The pregnant woman stands antisyphilitic therapy very well, the incidence of arsenical reactions being lower than in her nonpregnant syphilitic sister.

TREATMENT OF PRENATAL SYPHILIS

The best treatment, and likewise the correct treatment, of prenatal syphilis consists in the prophylaxis of the disease through discovering the mother's difficulty early and instituting adequate, continuous therapy up to the birth of the child. However, all too often the disease is discovered late or is never recognized until the birth of the child. In a way, such syphilis may be looked on as comparable to acquired syphilis in the secondary stage. It is generalized; the patient has built up little or no immunity to the process. Moreover, the lesions are of a high degree of virulence, so that from both the infant's standpoint as well as that of the public health it is essential that the disease be put under control as early as possible. For this purpose there is no drug to compare with the arsenicals. At Western Reserve University the drug neoarsphenamine is dissolved in from 2 to 3 cc. of distilled water and deposited under the loose tissues on the side of the scalp, next to the fascia. It is given in a beginning dose of 0.005 Gm. per kilogram and worked up to a maximum of 0.01 Gm. per kilogram. There is very little local reaction and the tissues of the buttocks are conserved for heavy metal

7. Moore, J. E.: Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, 1933, pp. 250-254.

8. Cole, H. N., and others: Cooperative Clinical Studies in the Treatment of Syphilis, J. A. M. A. **106**: 464 (Feb. 8) 1936.

injections. Moore prefers sulfarsphenamine in a beginning dose of 0.015 Gm., worked up to a maximum of 0.025 Gm. per kilogram. He feels that babies stand the therapy better than adults. He advises giving the injection concentrated in from 2 to 3 cc. of distilled water in the buttocks. Others are fearful of its use and employ Bismarsen N. N. R. (bismuth arsphenamine sulfonate) in a dose of 0.005 Gm. up to 0.01 Gm. per kilogram injected intramuscularly in 2 cc. of sterile distilled water. The infant may be given a course of from eight to ten such injections, followed immediately by a series of intramuscular injections of a bismuth salt; e. g., bismuth subsalicylate 2 mg. per kilogram for a total of eight injections. On the other hand, if injections are given twice a week one may employ in appropriate dose bismuth sodium tartrate, or iodobismitol. If desired, one may employ in place of the bismuth 1 Gm. of Strong Mercurial Ointment placed each day on the inner surface of the abdominal binder. The old fashioned mercury with chalk by mouth is prone to upset the stomach, though it may be tried occasionally as a course, from one-sixth to one-third grain (10 to 20 mg.), being given three times a day. The patient

Mercury with Chalk

℞ 100 pills, Mercury with Chalk..... 0.01 to 0.02 Gm.
Signa: One, three times a day.

should receive at least four or five courses of the arsenical and of the alternating heavy metal. The blood Wassermann test should be taken several times a year and a lumbar puncture should be performed at the end of one year of treatment. As a rule, treatment should be kept up until the blood Wassermann and spinal fluid reactions have been negative for one year. As yet I am unwilling to recommend the indiscriminate use of acetarsone by mouth in the treatment of congenital syphilis. It is still too much in the experimental stage.

With late prenatal syphilis one is dealing with a disease to which the body has worked up a definite immunity. It is true that there are specific problems with this phase of prenatal syphilis; e. g., interstitial keratitis and syphilis of the central nervous system. Otherwise, the patient may be treated much as one with latent acquired syphilis, the arsenicals being used in dosage comparable to the weight of the individual. Potassium iodide or sodium iodide is indicated in these cases. Moreover, the treatment of late prenatal syphilis must be looked on as a possible prophylactic of more severe complications; e. g., of the central nervous system, eighth nerve deafness or interstitial keratitis.

In patients with interstitial keratitis it is essential that the diagnosis be made as early as possible and energetic alternating courses of neoarsphenamine or of arsphenamine or of Mapharsen, with bismuth be employed. For the bismuth, Moore sometimes substitutes intramuscular injections of mercuric succinimide 0.01 Gm. Potassium or sodium iodide is given in large doses from 2 to 6 Gm. a day, in old cases with scars, not in acute cases. Naturally, local therapy also is indicated. If the keratitis is seen in the early stages, it generally responds to this therapy. In older cases there may be more or less scar formation and difficulty with vision. It is well to continue the alternating arsenical and heavy metal therapy for at least two years. This may be the means of obviating relapses or of preventing possible extension to the other eye. Many times nonspecific therapy has been most helpful in the treatment of resistant keratitis; e. g., the intramuscular injection of boiled milk or the intravenous injection of typhoid-paratyphoid vaccine. One may start with a dose of 1,000,000 and repeat in three hours, doubling the dose with each double injection and administering it every three or four days, for a series of from five to ten chills. Malaria therapy is especially valuable in old resistant keratitis, and I have seen it succeed when all other measures failed.

Involvement of the central nervous system in early or late prenatal syphilis is almost a problem to itself. The measures advised with acquired syphilis may be used. In juvenile tabes or dementia paralytica the outlook is very guarded. Even though the disease is checked there is usually little left except a vegetative animal. In other forms the response to therapy may be quite good. It is not advisable to use tryparsamide in prenatal syphilis; there is too much danger of misunderstanding and of damage to the optic nerve.

CONCLUSIONS

The best treatment for all forms of syphilis is prophylaxis. This can be achieved by better education of the public and of the physician, by the routine use of the Wassermann test or of similar flocculation tests in all our patients, especially in pregnancy when repeated tests should be made throughout the pregnancy. Moreover, routine Wassermann tests of all children would obviate much interstitial keratitis and eighth nerve deafness. Once syphilis has been discovered it should be thoroughly treated with arsenicals, bismuth preparations or mercury, exhibited in alternating continuous courses. The average cases of early syphilis require at least thirty injections of an arsenical and a like amount of heavy metal, and treatment should be kept up for one year after all signs and symptoms of the disease have disappeared. As explained in the text, appropriate measures must be adopted for syphilitic involvement of certain tracts or of special organs.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

AIRNET AIR FILTER ACCEPTABLE

Manufacturer: Airnet Air Filter Company, Chicago.

The Airnet Air Filter is designed to filter the outside air, eliminating a large percentage of the pollen, dust and dirt, for the relief of symptoms of hay fever. It is especially adapted for use in any ordinary room in home, office, hotel or hospital.

Airnet Air Filter.

The portable metal cabinet used is 24 inches wide, 12 inches high and 12 inches deep. There is a triple louver in the back to keep out rain or snow. The unit has a 9 inch circular opening in the center of the front of the cabinet through which the filtered air is discharged into the room. Its shipping weight is 75 pounds.

A motor manufactured by a well known concern and fitted with a propeller type fan is used in this unit. The motor and fan are mounted in a tube 9 inches in diameter and 6 inches deep. This tube concentrates the filtered air and forces it through the opening in the front of the cabinet.

A double filtering unit 2½ inches wide, about 12 inches high and about 24 inches wide fits in the back of the cabinet. The outside air is drawn through openings in the back of the cabinet and then through the double filtering unit. There is an air space of about 2½ inches between the two filters. This

air space between filters leads to efficiency, in the opinion of the firm, because it is more difficult for pollen, dust and dirt to pass the second filter.

The Airnet Air Filter supplies approximately 300 cubic feet of air per minute and uses about the same amount of current as a 40 watt lamp. It can be attached to any electric socket, alternating or direct current.

The manufacturer submitted evidence showing that more than 95 per cent of the pollen was eliminated by means of this unit and its cellulose filter. The device was tried in an institution acceptable to the Council and the firm's submitted evidence was verified.

In view of the favorable report, the Council voted to include the Airnet Air Filter in its list of accepted devices.

Council on Foods

THE COUNCIL ON FOODS HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

FRANKLIN C. BING, Secretary.

THE NUTRITIONAL SIGNIFICANCE OF GELATIN

Experimental investigations of the nutritive value of gelatin were begun early in the nineteenth century. A considerable mass of evidence has accumulated since that time. The older experiments, including the contributions of Voit and of Murlin on the so-called protein sparing action of gelatin, have been reviewed by Lusk[1] and others. In recent years much attention has been directed to the amino acid makeup of gelatin. The results of laboratory work have been reflected in advertising copy and in popular articles on nutrition. As might be expected, publicity that is promulgated by biased or scientifically untrained persons has been both favorable and unfavorable and, in the opinion of the Council, frequently has been misleading. Thus it has been stated that because gelatin is biochemically classed as an incomplete protein, lacking in certain essential amino acids, it is a food that should be avoided. And the use of gelatin as a means of increasing the protein content of the diet has been recommended just as enthusiastically as its use as a food has been condemned. Since the discovery of the dramatic success that has been reported to be attendant on the prescribing of aminoacetic acid to patients with certain myopathies, the advertising of one firm in particular has called attention to the relatively high proportion of this amino acid in gelatin and has suggested the use of gelatin in the treatment of muscular dystrophies. Gelatin has been recommended also for inclusion in the diet of infants. In the present report the Council has endeavored to evaluate the nutritional claims made for this food in the light of available evidence.

Preparation and Composition of Gelatin.—Gelatin is a protein derived from the collagen present in white fibrous tissue. It can be obtained from tendon, cartilage, bone and skin by boiling with water. This process is usually referred to as "hydrolysis," although there is some evidence that the changes involved are physical rather than chemical. There are several methods in common use for the commercial preparation of gelatin. Cow skins and trimmings are usually steeped for several weeks in a solution of lime water, then washed and boiled with water. Pig skins and trimmings are subjected to a preliminary treatment with acid. Bones are treated to remove the fat and mineral constituents, and the organic residue is largely converted into gelatin by boiling with water. Fish skins are a minor source of gelatin; they require only treatment with water to alter the collagen. Regardless of the source, there is obtained by appropriate preliminary treatment an aqueous solution containing gelatin. This is filtered, the water is evaporated, and the dried product is broken up and ground.

Gelatin is graded chiefly according to physical characteristics such as viscosity and jelly strength. These properties depend largely on the source of the gelatin and the method of manufacture. Different lots are therefore often tested and blended to make uniform products of the desired grade.

1. Lusk, Graham: The Elements of the Science of Nutrition, ed. 4, Philadelphia, W. B. Saunders Company, 1928, pp. 190, 365-367.

The dried gelatin usually consists of 85 to 90 per cent pure protein. A typical analysis of gelatin is recorded in table 1. The values for a powdered gelatin dessert are also listed because many persons think that the two products are almost identical.[2] It may be noted that the prepared gelatin dessert powders contain only about 10 per cent gelatin. Gelatin desserts can be prepared from edible gelatin as well as from the prepared mixtures; this may be advantageous in the preparation of low carbohydrate diets because of the possibility of omitting sugar from the final product.

Edible gelatin may contain traces of heavy metals which are present in the animal tissues from which the gelatin is derived. In order to guard against contamination during the manufacturing process the federal Food and Drug Administration has established certain limits of tolerance for arsenic, lead and copper in gelatin and other foods. These tolerances have been adopted also by the Council on Foods.

Gelatin as a Source of Protein in the Diet.—Many investigations over a period of years have brought out the significant fact that the nutritive value of proteins is measured largely by their digestibility and their amino acid makeup. It is interesting to note the occasional statement from prejudiced sources that because gelatin is obtained by partial hydrolysis it is partly digested to begin with and therefore is easily digested when eaten. Of course gelatin is readily digested by the proteolytic enzymes of the alimentary tract; but from the practical point of view the ready digestibility of gelatin does not confer on it any superiority over the common proteins.

The most extensive analysis of gelatin for amino acids is that reported by Dakin in 1920. His figures, which were

TABLE 1.—*Typical Analyses of Gelatin and Gelatin Dessert Powder*

	Gelatin, per Cent	Gelatin Dessert Powder, per Cent
Moisture	10.0	0.8
Ash	1.2	0.2
Fat (ether extract)	0.0	0.0
Protein (N × 5.5)	88.5	11.0
Carbohydrates	0.0	86.0
Tartaric or citric acid	none	2.0
Added flavor	none	present
Added color	none	present
Calories per gram (approximate)	3.5	3.9

based largely on the isolation of the individual amino acids, are recorded in table 2, together with additional data obtained by later investigators.[3] It is interesting to note that the sum of the nitrogen in the form of the various amino acids, plus the ammonia nitrogen reported by Dakin, amounts to 91 per cent of the nitrogen of gelatin. From the standpoint of our present knowledge of protein composition, this means that the amino acid makeup of gelatin is well known. The figures show that a number of amino acids have not been found in gelatin or are present in very small concentration. Valine, isoleucine, hydroxyglutamic acid and tryptophane are lacking. Tyrosine, cystine and methionine are present in small amounts. According to the results obtained in the feeding experiments of Rose and his collaborators, the essential amino acid which was later identified as alpha-amino-beta-hydroxybutyric acid[4] (and now called threonine[5]) is present in much smaller amounts in gelatin than in the casein of milk.[6] To date the following amino acids have been shown by feeding experiments with animals to be essential for growth: leucine, isoleucine, histi-

2. The values of gelatin are from the analysis published in THE JOURNAL Feb. 27, 1932, p. 737, and of the powdered gelatin dessert from the analysis published May 12, 1934, page 1566.

3. The references to the investigators named in table 2 are as follows:
Dakin, H. D.: J. Biol. Chem. **44:** 499 (Nov.) 1920.
Looney, J. M.: J. Biol. Chem. **69:** 519 (Aug.) 1926.
M. T. Hanke (J. Biol. Chem. **66:** 489 [Dec.] 1925) found 0.25 per cent in commercial gelatin.
Folin, Otto, and Looney, J. M.: J. Biol. Chem. **51:** 421 (April) 1922.
Jones, D. B.; Gersdorff, C. E. F., and Moeller, O.: J. Biol. Chem. **62:** 183 (Nov.) 1924.
Baernstein, H. D.: J. Biol. Chem. **97:** 663 (Sept.) 1932.
May, C. E., and Rose, E. R.: J. Biol. Chem. **54:** 213 (Oct.) 1922.
Bergmann, Max: J. Biol. Chem. **110:** 471 (July) 1935.

4. McCoy, R. H.; Meyer, C. E., and Rose, W. C.: J. Biol. Chem. **112:** 283 (Dec.) 1935.

5. Meyer, C. E., and Rose, W. C.: J. Biol. Chem. **115:** 721 (Oct.) 1936.

6. Ellis, R. H., and Rose, W. C.: J. Biol. Chem. **94:** 167 (Nov.) 1931.

dine, lysine, cystine or methionine,[7] phenylalanine, tryptophane and threonine. Future investigation may show that the animal body is incapable of synthesizing other amino acids.[7a] According to available data, gelatin may be classed as an incomplete protein because it lacks or contains too low a concentration of isoleucine, tryptophane and methionine.

It is the opinion of the Council that the amino acid composition of gelatin is of no practical disadvantage unless gelatin is the sole source of protein in the diet. The essential amino acids that are lacking in gelatin can and should be obtained from other sources in the diet. No one would attempt to live on a diet in which gelatin forms the sole source of protein. As a matter of fact, several investigators have attempted this feat as a scientific experiment without success. Kauffmann[8] reported in 1905 some feeding experiments in which he derived nitrogen entirely from gelatin supplemented with tyrosine, cystine and tryptophane and remained in nitrogen balance for a few days. His experiments, however, are inconclusive and are of historic interest only.

Gelatin, because of its swelling properties, cannot be eaten readily in the dry form or sprinkled on cereal. It is usually consumed as a solution which, if the concentration of gelatin is approximately 1 per cent or more, forms a gel on cooling. An ordinary serving of a gelatin dessert contains about 2.5 Gm. of gelatin. Recipes have been suggested in which a concentration of gelatin as high as 10 per cent may be prepared in the form of hot soups. It requires considerable ingenuity, however, to formulate a menu that contains more than about an ounce of dry gelatin per day.

Much information of lasting value has been gained through experimental studies of the nutritive advantages and disadvantages of gelatin. The report by Jackson and his collaborators[9] includes a review of the work to 1929 on the supplementary value of gelatin added to other proteins in the diet of rats. Thus it has been shown by Osborne and Mendel[10] that gelatin, which contains a relatively high concentration of lysine, will supplement gliadin, which contains about one-tenth as much of this essential amino acid. However, the application of these observations to human nutrition is obscure. The human being does not ingest synthetic diets, and an actual deficiency of lysine in the diet has never been demonstrated.

The suggested use of gelatin (containing 25 per cent of aminoacetic acid) in the treatment of the myopathies has already been mentioned. The dosage of aminoacetic acid in the treatment of myasthenia gravis or pseudohypertrophic muscular dystrophy usually is from 20 to 30 Gm. It should be apparent that gelatin can furnish only a small proportion of the proper dosage of this amino acid. In the opinion of the Council it is improper for manufacturers to exploit gelatin in connection with the observations on the use of aminoacetic acid in the treatment of the myopathies. Even if it were possible to secure appreciable quantities of aminoacetic acid by eating large quantities of gelatin, the recommendation to do so is objectionable. Each patient requires a specific amount and, in the opinion of the Council, to try to take aminoacetic acid in the form of gelatin would not only be haphazard but in many cases ineffective.

Other Uses of Gelatin of Interest in Nutrition.—Because of its characteristic physical properties, gelatin has a number of uses in the food industry. For example, it is customary to incorporate about 0.5 per cent of gelatin in many ice cream mixtures.[11] It is added in order to improve the "smooth" consistency of the product by enhancing its ability to be whipped and in other ways. Gelatin may also be an important ingredient of confections such as marshmallows.

Effect of Gelatin on Digestibility of Milk.—Of particular interest to physicians is the evidence regarding the effect of the addition of gelatin to milk. This has been supposed to increase the digestibility of the milk and in the past the use of gelatin in infant feeding was looked on with favor among pediatricians. It has been thought that gelatin as a colloid would coat the newly formed casein curds in the stomach and prevent their coalescence into larger curds. Some evidence has been obtained which indicates that the curd formed when milk plus gelatin is treated with acid tends to be softer than the curd formed with milk alone plus acid.

Clinical studies of the value of gelatin in infant feeding have yielded questionable or conflicting results. Julius Hess and Chamberlain[12] reported an outpatient study on infants fed gelatin. The gelatin was well tolerated but there was a tendency toward the formation of foul smelling, firm stools which were grayish yellow and which at times were passed with difficulty. Other infants receiving egg yolk in place of gelatin passed stools which were more plastic and in general were canary colored. Perlman[13] observed a slightly higher growth rate in infants fed gelatin than in infants fed the same diet without gelatin. From the observations reported by Elterich, Boyd and Neff[14] as a result of a careful study of eleven infants under hospital supervision, it may be concluded that gelatin does not specifically accelerate growth but may increase the caloric intake.

The use of gelatin in the form of an isotonic solution which also contained dextrose and sodium chloride has been suggested by Kugelmass[15] and by Halpern[16] for the prevention of weight losses in the first few days of life of new-born babies. Senn,[17] however, while confirming the fact that loss in weight is not so great when this solution is used, concluded that it is not a safe therapeutic procedure because it occasionally gives rise to edema formation and fails to prevent dehydration fever.

TABLE 2.—*Amino Acids in Gelatin*

	Dakin	Other Investigators
Aminoacetic acid	25.5	25.7 (Bergmann)
Alanine	8.7	
Valine	0	
Leucine	7.1	
Isoleucine	0	
Serine	0.4	
Phenylalanine	1.4	
Tyrosine	0.01	0 (Looney; Hanke)
Proline	9.5	19.7 (Bergmann)
Hydroxyproline	14.1	14.4 (Bergmann)
Aspartic acid	3.4	
Glutamic acid	5.8	
Hydroxyglutamic acid	0	
Histidine	0.9	
Arginine	8.2	
Lysine	5.9	
Cystine		0.16 (Looney; Folin and Looney; Jones, Gersdorff and Moeller)
Methionine		0.97 (Baernstein)
Tryptophane		0 (Looney; Folin and Looney; Jones, Gersdorff and Moeller; May and Rose)

Allowable Claims for Gelatin.—In view of the available evidence the Council believes that gelatin properly made is a wholesome food, that it has special usefulness when one desires to add variety to the diet by incorporating gelatin in nutritious soups or pleasant desserts which appeal to the appetite of many persons, and that for these reasons gelatin is often a useful food for inclusion in the diet of healthy persons or of sick or convalescent patients. Gelatin appears to be well tolerated. The claim that gelatin is an aid in the digestion of milk, however, is in the opinion of the Council not established. The claim that gelatin is of value as a source of aminoacetic acid in the treatment of some of the myopathies cannot be recognized; in the light of present evidence, gelatin has no special significance as a source of amino acids in the diet. Indeed, it is notoriously deficient in certain essential amino acids.

7. There is conclusive evidence that methionine can replace cystine; at the present time it is doubtful whether cystine can replace methionine.

7a. W. C. Rose and his collaborators have reported before the 1936 meeting of the Society of Biological Chemists that valine, an amino acid not present in gelatin, is indispensable in the diet.

8. Kauffmann, M.: Arch. f. d. ges. Physiol. **109:** 440, 1905.

9. Jackson, R. W.; Sommer, B. E., and Rose, W. C.: J. Biol. Chem. **80:** 167 (Nov.) 1928.

10. Osborne, T. B., and Mendel, L. B.: J. Biol. Chem. **13:** 233, 1912-1913.

11. Rogers, L. A., Associates of: Fundamentals of Dairy Science, ed. 2, American Chemical Society Monograph Series, New York, Reinhold Publishing Corporation, 1935, p. 264.

12. Hess, J. H., and Chamberlain, I. McK.: Gelatin Added to Diets of Artificially Fed Infants, J. A. M. A. **89:** 1423 (Oct. 22) 1927.

13. Perlman, H. H.: Arch. Pediat. **45:** 14 (Jan.) 1928.

14. Elterich, T. O.; Boyd, D. H., and Neff, Andrew: Arch. Pediat. **47:** 286 (May) 1930.

15. Kugelmass, I. N.; Berggren, R. E. L., and Cummings, Mildred: Preventing Loss of Weight in the New-Born, Am. J. Dis. Child. **46:** 280 (Aug.) 1933.

16. Halpern, L. J.: J. Pediat. **5:** 40 (July) 1934.

17. Senn, M. J. E.: J. Pediat. **7:** 352 (Sept.) 1935.

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SATURDAY, DECEMBER 26, 1936

RESPIRATORY IRRITANTS: THEIR EFFECTS AND PREVENTION

Little has been written on the influence of soot on the development of tumors of the lungs. The concentration of coal smoke in most of the large cities in this country, however, is such that it is important to determine the effects of this daily contamination of the inspired air. Seelig and Benignus [1] have reported an experimental study dealing with the carcinogenic power of soot on the lungs. They endeavored to determine whether or not the soot deposited out of coal smoke played a part in the development of tumors of the lung in white mice. The soot used in the experiments was secured by sweeping the flue of a hospital furnace that burned Kentucky bituminous nut coal, and it was substituted for sawdust and shavings as a bedding material for the mice. Dust from the soot was raised by the normal activity of the mice, but in addition each cage was violently shaken two or three times a day. The principal constituents of the soot were silica, tarry matter, sulfur and volatile salts, including ammonia. One hundred mice were subjected to this atmosphere of soot dust, and fifty controls were kept under normal laboratory conditions at a distance from the cages containing the experimental animals. The animals of both groups were about 3 months old. As each mouse died, a necropsy was performed, except on the thorax, after which the mouse was placed in 10 per cent solution of formaldehyde with the lungs in situ. After three or four days the lungs were removed, embedded in paraffin and sectioned serially. At the end of six months, 20 per cent of both groups had died. At the end of a year, about 60 per cent of the animals in both groups had died, and at the end of eighteen months all the animals had succumbed. The histologic study showed that in the control group of fifty mice there was only one with adenocarcinoma of the lung, an incidence of 2 per cent. In contrast to this, eight mice in the experimental group showed adenocarcinoma of the lung, an incidence of 8 per cent. In two additional mice there were tumors resembling bronchiogenic carcinomas, but these were eliminated since they could not be differentiated from active nonmalignant intrabronchial hyperplasia.

Since the mice subjected to soot dust showed an incidence of lung cancer four times as great as the control group, the next question was What is the comparative incidence of human cancer of the lung in urban and rural communities? The available data were tabulated for the authors by Dr. Halbert L. Dunn of the United States Bureau of the Census. Although a consistent and markedly higher death rate in the cities is noted in these tables, too many factors enter into an interpretation of the census figures to permit dogmatic conclusions. These figures provide sufficient evidence, however, to show the necessity for further studies of the subject.

Coal dust is not the only irritative constituent of the air that may be a menace to the public health. Some problems of respiratory protection in the petroleum industry have been discussed by Kintz and Fowler [2] of the U. S. Bureau of Mines. An atmosphere is dangerous when it contains one or more foreign substances, such as gas, dust, mist or fumes, in sufficient quantity to be harmful or explosive, or when it does not contain enough oxygen to allow working with maximum efficiency or to support life, or when the temperature and humidity are too high for human endurance. Satisfactory solution of problems created by atmospheric conditions that are unsafe or detrimental to the health and efficiency of workers can be reached, these writers say, only after careful analysis of individual circumstances. The specific impurity in the air to which each worker on each job is exposed must be determined, its dangers recognized, and effective protective measures taken—measures that not only protect but offer a minimum of inconvenience to the worker.

Some methods for determining the relative harmlessness of atmospheric conditions are available. Detectors for inflammable gas, toxic gas, pyrotannic acid, carbon monoxide and hydrogen sulfide are available. Deficiency in the oxygen content of the air can also be determined. Instruments are available for counting and recording the amount of dust in the air. The most satisfactory procedure when possible is to render the inspired air harmless. Under some circumstances this does not seem to be always possible. When it is necessary for individuals to live under dangerous atmospheric conditions, the oxygen supply and the nature and degree of harmfulness of the toxic substances in the air should be known as accurately as possible. Such protective equipment as the canister-type gas mask, dust respi-

1. Seelig, M. G., and Benignus, E. L.: Coal Smoke Soot and Tumors of the Lung in Mice, Am. J. Cancer **28**: 96 (Sept.) 1936.

2. Kintz, G. M., and Fowler, H. C.: Some Problems of Respiratory Protection in the Petroleum Industry, with Suggestions for Their Solution, U. S. Bureau of Mines Information Circular 6915, November 1936.

rators, self-contained oxygen breathing apparatus, hose masks and air-line respirators may serve a limited purpose.

Intense interest has been stimulated in certain quarters in the problems of respiratory irritants, and factual data are rapidly accumulating. The interest also of those not technically employed in this field should be stimulated toward the public health problems involved.

LOSS OF CEVITAMIC ACID

Once the constitution and chemical nature of vitamin C (cevitamic acid) were established, it became possible to develop strictly chemical methods for determining this dietary essential in food materials, tissues and body fluids. The most widely used method employs the readily reduced organic compound 2,6 dichlorophenol indophenol as an indicator; the specificity of the reaction as well as the comparison of the results so obtained with the time-consuming bio-assay on guinea-pigs has received careful attention. The wide usefulness of the titration method has been demonstrated. Thus, not only is it possible to note changes in the vitamin C content of foods as a result of processing—cooking, pasteurization, storage—but the localization of cevitamic acid in certain animal tissues and the variations in its concentration in blood and urine can be determined in a relatively short time.

That the content of this dietary essential in the plasma parallels its content in the urine has been indicated by Greenberg, Rinehart and Phatak.[1] The average value for plasma vitamin C in twenty-five normal human subjects excreting more than 50 mg. in the urine was 0.92 mg. per hundred cubic centimeters, whereas thirteen subjects excreting less than 50 mg. had 0.44 mg. per hundred cubic centimeters in the plasma. The responsiveness of plasma concentration to intake is shown by the appreciable rises (from 15 to 69 per cent) in plasma level within two to four hours after the ingestion of 6 ounces of orange juice. The thirty-eight normal subjects were further classified into groups according to the approximate antiscorbutic value of their diet. The cevitamic acid content in the plasma of the eleven subjects rated as low was found to be 0.55 mg. per hundred cubic centimeters; of the nineteen rated as fair, 0.75 mg., and of the eight rated as good, 1.10 mg.

These studies show the wide variation in the vitamin C content of the blood of so-called normal individuals and the close correlation with the amount ingested. That the foregoing relationships merit attention in the clinic is emphasized by the recent observations of Daniels and Everson[2] that ingestion of acetylsalicylic acid is followed by a pronounced increase in cevitamic acid in the urine. Thus, on a constant dietary regimen, four children given 2½ grains (0.16 Gm.) of the drug showed from 100 to more than 200 per cent increase in the loss of vitamin C in the urine. It is obvious that, in certain cases in which prolonged administration of acetylsalicylic acid is required, particular attention must be given to the allowance of vitamin C lest scurvy appear. Doubtless other similar antagonisms exist. As the human requirement for most of the recognized indispensable accessory food substances is not known, it follows that, so far as possible, optimal nutrition should be maintained in treating the patient.

1. Greenberg, L. D.; Rinehart, J. F., and Phatak, N. M.: Proc. Soc. Exper. Biol. & Med. **35**: 135 (Oct.) 1936.
2. Daniels, Amy L., and Everson, G. I.: Proc. Soc. Exper. Biol. & Med. **35**: 20 (Oct.) 1936.

EXTRASYSTOLES

Extrasystoles, the most common cause of irregularity of the heart's action, were formerly regarded as a symptom of myocardial damage. A valuable part of Sir James Mackenzie's great work was the clinical differentiation between extrasystoles and auricular fibrillation; at the same time he showed the relative unimportance of the former and the importance of the latter. However, to deny any significance to extrasystoles would be to lose a sign which might help in diagnosis and treatment. According to Boas and Levy,[1] at least 50 per cent of patients with extrasystoles have normal hearts as far as can be determined. They occur in a large proportion of elderly men and not infrequently in young subjects. Mackenzie[2] noted premature beats in a man at the age of 69 in whom they were first discovered at the age of 18. This patient had earned a living at work that entailed great bodily strain and yet he was in fairly good health after fifty-one years with premature beats. Grassmann[3] reported a case in which they were known to be present for sixty-seven years. Extrasystoles are said to arise from an irritable focus in the musculature of the auricles or of the ventricles or from the auriculoventricular node. It is sometimes possible to differentiate clinically between the sites of origin. When extrasystoles originate in the auricle, the normal rhythm from the sino-auricular node is generally disturbed and there is no compensatory pause. When extrasystoles originate in the auriculoventricular node or in the ventricle, the sino-auricular rhythm is maintained. There is then a compensatory pause after the premature beat, and the intervals before and after it are together equal to two normal beats. When the extrasystole is ventricular, the auricular wave (P) in the electrocardiogram is uneffected in shape and position but may or may not be visible, owing to its inclusion in the ventricular complex (QRST).

1. Boas, E. P., and Levy, Hyman: Extrasystoles of Clinical Significance, Am. Heart J. **11**: 264 (March) 1936.
2. Mackenzie, James: Diseases of the Heart, London, Oxford University Press, 1913.
3. Grassmann, Karl: Zur prognostischen Wertigkeit und Behandlung der praktisch-wicktigsten Herzarrythmien, München. med. Wchnschr. **67**: 5 (Jan. 2) 1920.

The causes of extrasystoles are not always clear. There is slight support for the theory that they are more likely to arise in the cardiac area, where there is the greatest strain. Campbell [4] reported their presence in about 20 per cent of 500 consecutive cases in the cardiographic department at Guy's Hospital. About one fourth of these patients apparently had no heart disease whatever; another one fourth had rheumatic heart disease; pregnancy seemed to be the exciting cause in some cases. High blood pressure (over 170) accounted for 16 per cent, and myocardial or atheromatous changes for 18 per cent. A few cases were associated with exophthalmic goiter, with syphilitic arterial disease and with the administration of quinidine. Extrasystoles may be induced by smoking or by coffee, or by the administration of digitalis or the salicylates; such extrasystoles disappear when the offending agent is removed. Acute infections can be the immediate cause of extrasystoles. When they appear suddenly in the course of an acute infection it is an indication that the heart has been injured by the infectious process. Extrasystoles that arise in the auricles in patients with mitral stenosis are said to presage the appearance of auricular fibrillation. They may be closely linked with progressive disease of the coronary arteries, especially when they appear for the first time in middle age or later. Boas and Levy [1] observed a significant relationship between the occurrence of extrasystoles and of anginal attacks. In the records of 974 patients with coronary sclerosis, fifty-three had extrasystoles. Twenty-one per cent of these fifty-three patients had died, whereas only 10.4 per cent of the 921 patients with coronary disease without extrasystoles had died.

Extrasystoles are encountered less frequently as the heart rate becomes more rapid. They are exceedingly rare at heart rates of 120. For this reason they are unusual in febrile diseases and in hyperthyroidism. Physical exercise usually abolishes extrasystoles simply by accelerating the heart rate. Boas and Levy analyzed 183 cases in private practice that presented extrasystoles. In two thirds of these cases the heart rate was between 70 and 100. Ventricular extrasystoles did not occur in patients whose hearts were normal at heart rates above 110, and in only two instances (both children) did auricular extrasystoles occur at these rates. The great majority of their patients who had extrasystoles during rapid heart rates had definite myocardial disease. Extrasystoles were not present in patients with hyperthyroidism except in the presence of complicating heart disease and multifocal extrasystoles. In persons whose hearts are otherwise normal, extrasystoles do not portend present or future heart disease, and their appearance in frank heart disease usually does not add to the gravity of the prognosis.

4. Campbell, Maurice: The Etiology and Significance of Extrasystoles, Guy's Hosp. Rep. **79**: 142-158 (April) 1929.

Current Comment

PAINTING THE ORANGE

Today the orange is universally recognized as a rich source of vitamin C and therefore a desirable fruit for children. The natural color and other characteristics of the rind vary with different varieties and with the season. Once these features served to some extent as marks of identification. This is not true today, when there is current a tendency to "improve on nature." The inherent color of the rind of certain varieties of the orange is not an index of maturity of the fruit or of the degree of sweetness of the juice. Green pigment persists in the skin of mature fruit of high quality. Many growers apparently believe that the presence of chlorophyll in the pericarp impairs the marketability of the fruit. Several years ago the practice of exposing oranges to ethylene gas for from two to four days was introduced. The ethylene causes a blanching of the green color and a consequent unmasking of the yellow pigments also present in the skin. The United States Department of Agriculture has ruled that this process does not in itself constitute adulteration, and there is evidence that the nutritional value of the juice is not affected by it. More recently a rapid method of coloring has been employed. The fruit is dipped in a solution of a harmless coal tar dye, which gives to the resulting "painted oranges" a more uniform, brilliant color. Food laws require that the presence of dyes must be declared by having the phrase "color added" stamped on each orange. The staining of unripe or damaged fruit by any method in simulation of oranges of greater maturity or of superior quality constitutes adulteration under the Food and Drugs Act. The degree of maturity of the orange is determined by chemical analysis of the amount of sugar and citric acid in the juice. Unless there are eight parts of sugar to each part of acid, the fruit is held to be unripe and inferior. The state of Florida has recently provided rigid regulation of the packaging and marketing of citrus fruit according to more exacting standards than those required by the federal government. The United States Department of Agriculture accordingly has agreed to wait until September 1937 before action will be taken. Thereafter interstate shipments of inferior oranges that have been colored will be liable to seizure and destruction. The Florida regulations in large measure should serve to remove the necessity for federal action. Accurate information concerning the effect of the artificial coloring of oranges on the consumption of the fruit is not available. The phrase "color added" stamped on each stained orange has certainly puzzled alert housewives, many of whom under the direction of their family physician are buying oranges for the baby. Consumers have questioned whether the colored oranges are of high quality. They have tasted the juice warily and have inquired whether the vitamin content is as high as in the uncolored fruit. Some consumers have expressed the opinion that colored oranges do not keep as well as the untreated russet colored fruit. Others have asked whether the "painted" rind is suitable for

making marmalade and candied orange peel. These questions are evidence of intelligent interest on the part of the public. The promulgators of the coloring of oranges should arrange to answer them decisively by scientific evidence.

Association News

RADIO BROADCASTS

The American Medical Association and the National Broadcasting Company are presenting the second series of dramatized health broadcasts under the title Your Health. The first broadcast in the new series, the thirty-second dramatized cooperative broadcast under the title Your Health, was given October 13. The theme for 1936-1937 differs slightly from the topic in the first series, which was "medical emergencies and how they are met." The new series is built around the central idea that "100,000 American physicians in great cities and tiny villages, who are members of the American Medical Association and of county and state medical societies, stand ready, day and night, to serve American people in sickness and in health."

The program will go out on the Blue network instead of on the Red network, as originally announced.

The topics are announced monthly in advance in *Hygeia*, the Health Magazine, and three weeks in advance in each issue of THE JOURNAL. The topics and speakers for the next three programs are:

December 29. Health Assets and Liabilities. W. W. Bauer, M.D.
January 5. "Smog." W. W. Bauer, M.D.
January 12. Winter Health Hazards. W. W. Bauer, M.D.

The time of the broadcast is Tuesday afternoon at 4 o'clock central standard time (5 o'clock eastern time, 3 o'clock mountain time, 2 o'clock Pacific time).

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST; SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Annual Reregistration Due January 1.—Every licentiate of the Arkansas Eclectic Medical Examining Board must register annually with the secretary of the board between January 1 and the last day in February and pay a fee, if a resident of Arkansas, of $2 and, if a nonresident, of $4. The failure of a licentiate to pay the required fee by March 1 automatically suspends his right to practice while delinquent. If he fails for three successive years to pay the required fee, his license is to be cancelled, and thereafter he will be reinstated only on such a showing to the board of moral character and professional qualifications as would entitle the applicant to the issuance of an original license and the payment of the same fees as are required for the issuance of an original license.

CALIFORNIA

Plague Infection.—According to *Public Health Reports*, plague infection has been proved, by animal inoculation, in fleas taken from twenty-four ground squirrels, Citellus beechei fisheri, shot October 10, in Holcomb Valley, six miles north of Pine Knot, in San Bernardino County.

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in California is required by law to register annually, on or before January 1, with the secretary-treasurer of the board of medical examiners, and at that time to pay a fee of $2. Failure to pay the required fee within sixty days after January 1 works a revocation of a license and thereafter a license may be reissued only after application and the payment of a $10 penalty.

Society News.—Dr. David G. Ghrist, Glendale, addressed the San Diego County Medical Society, December 8, on "Differential Diagnosis and Treatment of Chronic Arthritis."——At a meeting of the San Diego Academy of Medicine, December 3, Dr. John H. Musser, New Orleans, was the guest speaker.——At a meeting of the staff of Peralta Hospital, Oakland, Drs. John W. Sherrick and Emery R. Ranker discussed chorio-epithelioma of an ovarian pregnancy and of the testis respectively, among other speakers.

Fifty-Fifth Series of Popular Lectures.—Stanford University School of Medicine, San Francisco, announces the fifty-fifth series of popular medical lectures to be given in Lane Hall on alternate Friday evenings during the winter quarter. Following is the schedule:

Dr. Jacques P. Gray, San Francisco, January 8, Syphilis and Its Control.
Dr. Benjamin W. Black, Oakland, January 22, The County Hospital and the Public.
Dr. William C. Voorsanger, San Francisco, February 5, Recent Advances in the Treatment of Tuberculosis.
Dr. Frederic C. Bost, San Francisco, February 19, The Crippled Child.
Sanford M. Moose, D.D.S., San Francisco, March 5, Behind the Scenes of Pain Relievers in Dentistry.
Dr. Jay Marion Read, San Francisco, March 19, The Rising Death Rate from Heart Diseases.

COLORADO

New Tuberculosis Research Laboratory.—A tuberculosis research laboratory has been established in Colorado Springs, to be operated by the Colorado Research Foundation assisted by scientists of the Colorado College. The laboratory was financed by the city of Colorado Springs and the PWA. It contains 3,000 square feet of floor space divided into twelve rooms including a monkey room, guinea-pig and rabbit quarters, five individual laboratories, x-ray room, spectrographic room, photographic dark room, director's office and sterilizing room.

CONNECTICUT

Annual Registration Due During January.—Every practioner of medicine and surgery holding a license to practice in Connecticut is required by law to register with the state department of health during January and at that time to pay a fee of $2. Licentiates who have retired from active practice or who live out of the state must register annually but need not pay a fee. A practitioner failing to register is liable to a fine of not more than $5.

Outbreak of Food Poisoning.—Eighteen orderlies and one ward maid at New Haven Hospital, New Haven, were attacked October 26 with diarrhea and abdominal cramps. The illness was self limited and all were clinically well within forty-eight hours. The etiologic factor was not established. Duplicate stool specimens from each patient failed to show any recognized pathogen. The source of the outbreak was not established, although it was assumed to be of food origin because of the simultaneous outbreak, and all those involved received their meals from one source. The personnel of the serving kitchen was also studied bacteriologically, but no pathogens were isolated. No subsequent cases developed.

DISTRICT OF COLUMBIA

Society News.—Dr. Garnet W. Ault addressed the Medical Society of the District of Columbia, December 16, on "Recent Advances in Proctology," and Frederick A. Fenning, counsel for the society, discussed "Court of Appeals Decisions, with Excerpts of the Evidence, in Cases Brought By and Against Washington Physicians." Dr. Samuel A. Levine, Boston, discussed "Pitfalls in the Diagnosis of Heart Disease" before the society, December 9, meeting jointly with the Washington Heart Association.——At a meeting of the Washington Ophthalmological Society, November 2, Drs. Alfred Bielschowsky, Hanover, N. H., spoke on "Etiology of Squint"; John W. Burke, "Papilloma of Canaliculus," and Leroy W. Hyde, "Hemangioma of the Orbit."

Study of Man and Environment.—The Academy of Medicine of Washington is planning an extended study of the medical aspects of the interaction between man and his environment. At a meeting, December 8, "The Reaction of the Individual to His Social Environment, with Special Reference to Emotions as a Factor in Disease" was presented by the committee in charge of this phase of the subject: Drs. Walter L. Treadway, assistant surgeon general in charge of mental hygiene, and Henry H. Hazen, both of the U. S. Public Health Service; Lewis C. Ecker, associate professor of medicine, Georgetown University Medical School; Earl B. McKinley, dean, George Washington University School of Medicine, and also from George Washington, Drs. Walter A. Bloedorn, professor of medicine, William J. Mallory, professor of medicine, and Vincent Du Vigneaud, Ph.D., professor of biochemistry.

GEORGIA

Society News.—Dr. Stacy C. Howell, Atlanta, among others, presented a paper before the Fulton County Medical Society in Atlanta, December 3, entitled "Action of Epinephrine on the Diseased Human Eye." Drs. F. Phinizy Calhoun and Thomas F. Sellers addressed the society on "The Intra-Ocular Invasion by the Larva of the Ascaris" November 19. The speakers November 5 were Drs. Amey Chappell and Frank Lee Bivings, among others, on "Blood Studies on Negro Women During Pregnancy."

ILLINOIS

In Memory of Dr. Rice.—A bronze plaque in the lobby of the Kane County Spring Brook Sanatorium, Aurora, was dedicated, December 6, to the memory of the late Dr. Imas P. Rice, superintendent, who died April 23. Dr. Rice, the first superintendent of the hospital, had held the position since March 10, 1921.

Society News.—Dr. Clark W. Finnerud, Chicago, addressed the DuPage County Medical Society in Naperville, November 18, on "Diagnosis and Treatment of Common Skin Diseases."——At a meeting of the Winnebago County Medical Society in Rockford, December 18, Dr. Edward L. Cornell, Chicago, spoke on "Newer Developments in Obstetrics."

Fifty Years in Practice.—The Adams County Medical Society held a special meeting and dinner, November 24, to honor Drs. Melinda C. K. Germann and J. W. Edward Bitter, who have completed fifty years in the practice of medicine in Quincy. Dr. J. Carl Steiner was toastmaster. Gold wrist watches were presented to both physicians. Speakers included Drs. Francis L. Reder, St. Louis, and Henry J. Jurgens, and three physicians who also have completed fifty years of practice: Drs. Levin H. A. Nickerson, Edmund B. Montgomery and William W. Williams. Dr. Germann graduated from the Quincy College of Medicine in 1886 and has been active in the civic life of the community. Dr. Bitter also graduated from the Quincy College of Medicine; he served two terms as president of the Adams County Medical Society in 1929 and 1933 and as secretary from 1922 to 1923.

Chicago

Rush Abolishes Fifth Year Requirement for Degree.—The faculty of Rush Medical College recently voted to abolish the requirement of the fifth year for the degree of doctor of medicine, effective December 15. Certain additional provisions were made for students who have received the four year certificate since 1934 and who never received their degree because of illness and for students who received the certificate in the past year who were either not under contract to a hospital or whose contract could be altered by the hospital concerned to permit them to receive their degree before completing their internships.

Society News.—Dr. Maurice F. Lautman, Hot Springs National Park, Ark., addressed the Chicago Medical Society, December 16, on "The Present Status of the Treatment of Arthritis," and Dr. Laurence H. Mayers, "Arthritis."——At a meeting of the Chicago Pathological Society, December 14, Dr. Edward L. Compere, among others, spoke on "Pathology of the Spine."——The Chicago Pediatric Society was addressed, December 15, among others, by John Hays Bailey, Ph.D., on "Observations on the Epidemiology of Certain Streptococcic Diseases."——At a meeting of the Chicago Society of Internal Medicine, December 15, the speakers included Dr. Walter J. R. Camp on "Influence of Epinephrine on the Distribution of Potassium in the Body."

INDIANA

Dr. Ferree Named Chief of Health Administration.—Dr. John W. Ferree, Bluffton, has been appointed chief of the newly created bureau of local health administration, Indiana State Division of Public Health, according to the state medical journal. Dr. Ferree, who graduated from the Indiana University School of Medicine, Indianapolis, in 1932, will supervise local health activities, help organize local departments and aid with the preparation of programs and budgets.

Society News.—Dr. Ernest R. Carlo, Fort Wayne, was chosen president of the Indiana Pediatric Society at its annual meeting in Fort Wayne, November 6-7. Dr. Harold D. Lynch, Evansville, was named vice president and Dr. Matthew Winters, Indianapolis, reelected secretary-treasurer.——Dr. David I. Schwartz addressed the Fort Wayne Medical Society, December 15, on "Treatment of Acute Hematogenous Osteomyelitis," and Dr. A. Jerome Sparks, December 1, "Management of Urinary Calculi."——Dr. Juan Rodriguez conducted an x-ray seminar before the Academy of Medicine and Surgery, Fort Wayne, December 8.——The St. Joseph County Medical Society was addressed at its fifty-first annual meeting in Mishawaka, November 18, among others, by Drs. Norman R. Kretzschmar, Ann Arbor, Mich., on "Antepartum Bleeding"; John deJ. Pemberton, Rochester, Minn., "Surgery of the Thyroid Gland," and Irving S. Cutter, Chicago, "Fight Against Puerperal Fever."——Dr. Willis D. Gatch, Indianapolis, discussed "Indications for Surgery in the Acute Abdomen" before the Carroll County Medical Society in Camden in November.——At a meeting of the Fayette-Franklin County Medical Society in Connersville, November 10, Dr. Gordon W. Batman, Indianapolis, spoke on "Early Diagnosis and Treatment of Congenital Deformities."——Dr. Byron G. Shaffer, Toledo, Ohio, addressed the Northeastern Indiana Academy of Medicine in Kendallville, November 19, on "The Surgical Aspect of Peptic Ulcer."

KANSAS

Society News.—At a meeting of the Rush-Ness County Medical Society in Ransom, October 1, Dr. Clyde D. Blake, Hays, discussed "Empyema and Its Management" and Dr. Lester A. Latimer, Alexander, "Conjunctivitis, Its Management and Treatment."——The Tri-County Medical Society was addressed in Wellington, October 14, among others, by Drs. Andrew B. Rivers, Rochester, Minn., on "Treatment of Peptic Ulcer" and "The Chronic Dyspeptic"; Ferdinand C. Helwig, Kansas City, Mo., "Pitfalls in Diagnosis and Treatment in Malignant Disease," and Nathaniel G. Alcock, Iowa City, the enlarged prostate.——Dr. Leroy A. Calkins, Kansas City, Mo., discussed "Menopause Menorrhagia" before the Sedgwick County Medical Society in Wichita, December 1. Dr. Olin West, Secretary and General Manager, American Medical Association, addressed a joint meeting of the society and its woman's auxiliary, December 15.

MASSACHUSETTS

Mental Hygiene Officers.—At the annual meeting of the Massachusetts Society for Mental Hygiene in Boston, November 24, Dr. Donald Gregg, Wellesley, was elected president; Walter F. Dearborn, Ph.D., Cambridge, vice president, and Dr. Charles E. Thompson, Gardner, secretary.

Anesthetists Oppose Hospital Prepayment Plan.—At a special meeting, November 6, the Boston Society of Anesthetists passed a resolution opposing a proposed hospital prepayment plan as it is now drawn up for consideration by Boston hospitals. The resolution declared that the present contract would tend to reduce anesthetists toward the position of technicians, place them under the control of the hospitals and set them apart from other branches of medicine. It further declared that the progress of anesthesia would be impaired and that poorer service to the patient would ultimately be the result. The resolution was passed after a series of conferences with anesthetists from New York, Rochester, Washington and other places held during the Congress of Anesthetists in Philadelphia during October.

MICHIGAN

Medical Director of Psychopathic Hospital.—Dr. Raymond W. Waggoner, associate professor of neurology, University of Michigan School of Medicine, Ann Arbor, has been appointed medical director of the state psychopathic hospital to succeed the late Dr. Albert M. Barrett, who held the position for thirty years. Dr. Waggoner, who is 35 years of age, is an alumnus of the university medical school.

Society News.—Dr. Robert S. Breakey, Lansing, addressed the Shiawassee County Medical Society, October 15, on renal calculi.——Samuel Lewis, D.D.S., addressed the Detroit Pediatric Society, December 2, on "Indications and Contraindications for Orthodontic Treatment in Children."——Dr. Edward Cathcart, Detroit, addressed the Oakland County Medical Society in Pontiac, November 17, on "The Association of Renal Neoplasms with Calculi."——At a joint meeting of the Muskegon and Kent county medical societies in Grand Rapids, November 18, Dr. Russell M. Wilder, Rochester, Minn., spoke on "Clinical Investigation of the Action of Protamine Insulin."——Ernest O. Melby, Ph.D., dean, school of education, Northwestern University, Evanston, Ill., discussed "Recent Trends in Education" before the Calhoun County Medical Society in Battle Creek, December 1.——Dr. Harold G. Pudleiner, Battle Creek, addressed the Saginaw County Medical Society, November 17, on hydronephrosis.

MINNESOTA

Annual Registration Due During January.—Every practitioner of medicine and surgery holding a license to practice in Minnesota is required by law to register annually during January, with the secretary of the board of medical examiners, and at that time to pay a fee of $2. A licentiate who practices without renewing his license is guilty of a misdemeanor and is liable to prosecution.

The Bell Lecture.—Dr. Harry E. Kleinschmidt, director of health education service, National Tuberculosis Association, New York, delivered the third annual J. W. Bell Lecture of the Hennepin County Medical Society, December 7. His subject was "The Doctor and Tuberculosis of the Future." The lectureship was established as a memorial to the late Dr. John W. Bell and each year serves as a tribute to him and to one other outstanding physician. This year the lecture commemorated Dr. Frederick A. Erb, who died October 25 while president of the Hennepin County Tuberculosis Association.

Society News.—Dr. Martin Nordland, Minneapolis, discussed surgical lesions of the neck before the Kandiyohi-Swift-Meeker Medical Society at Willmar, October 27.——At a meeting of the Rice County Medical Society in Faribault, October 1, Dr. Alfred W. Adson, Rochester, spoke on "Diagnosis and Surgical Treatment of Spinal Cord Tumors."——At a meeting of the Upper Mississippi Medical Society in Bemidji, October 31, among others, Dr. Oscar E. Locken, Crookston, read a paper entitled "Will the Government or the Patient Pay?" and Dr. L. Strausman, Rochester, "State Medicine as Seen in Germany."——Dr. David E. McBroom, Cambridge, was chosen president of the Minnesota Medical Officers' Association at its annual meeting, October 5; Dr. Ethel R. Beede, Faribault, vice president, and Dr. Herman E. Hilleboe, St. Paul, secretary; Dr. Arthur R. T. Wylie, Faribault, discussed feeblemindedness.

Delegates Reaffirm Free Choice of Physician.—Following a special meeting of the house of delegates of the Minnesota State Medical Association, November 1, the committee on public policy and legislation issued a statement to the interim committee on social security legislation of the Minnesota state legislature defining the position of the association on the medical aspects of relief. The statement reaffirmed the association's belief in the principle of free choice of physician by the recipient of relief or his guardian and preservation of the traditional physician-patient relationship. "We also believe," the statement said, "that where local private hospital facilities are available, adequate and practicable, the recipient of relief or his guardian should have the choice of hospital." Strong opposition was expressed to the practice of "bidding" for the rendering of medical services. This kind of service is not conducive to the best interests of the patient, the taxpayer or the medical profession, and free choice of physician with a reasonable allowance to the physician for his services will eliminate it, the delegates believe. The statement expressed the association's opinion that each case should be considered on its merits. It was the opinion of the spokesmen that the allowance for medical services to recipients of relief should be paid directly to the physician. They assured the interim committee that the association as a body is willing to administer to those who are unable to provide medical attention for themselves and that it wishes to cooperate with the legislature in the future as in the past. It is willing to continue the plan of medical advisory committees selected by the county medical societies to assist local relief authorities in medical matters, believing that this plan has functioned satisfactorily. The statement also recorded approval of the present forms of authorization for medical service.

MISSOURI

Memorial Meeting.—The Jackson County Medical Society, Kansas City, held a memorial meeting in honor of the late Dr. Emsley T. Johnson, December 8. Dr. Johnson was the president-elect of the society. He died suddenly of a cerebral hemorrhage, November 20.

State Prison Quarantined for Smallpox.—Newspapers reported November 27 that the Missouri state prison at Jefferson City had been under quarantine since October 15 on account of an outbreak of smallpox. Up to November 27 seven cases had been reported. There are about 4,800 inmates in the prison.

Society News.—The St. Louis Medical Society was addressed, December 9, by Drs. Cyril M. MacBryde on "Insulin Response as an Index to the Dietary Management of Diabetes"; Duff S. Allen, "Effect of Goiter and Thyroidectomy in the Aged," and August A. Werner, "Relationship of Thyrotropic Hormone to Exophthalmic and Toxic Adenomatous Goiter."——Dr. Richard L. Sutton Jr., Kansas City, addressed the Jasper County Medical Society at Joplin, November 17, on "Common Diseases of the Skin."——At a meeting of the Kansas City Dental Society, December 14, Dr. Russell L. Haden, Cleveland, presented "Reflections on the Focal Infection Problem."——Dr. Austin A. Hayden, Chicago, secretary, Board of Trustees, showed a motion picture film of the activities of the American Medical Association before the Jackson County Medical Society, December 15.——Dr. Ulysses S. Short discussed "Allergy and Its Nasal Manifestations" at a joint meeting of the St. Louis County Medical Society and its woman's auxiliary, November 24.

NEW YORK

Hospital Insurance for Western New York.—The Hospital Service Corporation of Western New York will go into operation Jan. 1, 1937, with headquarters in Buffalo. Carl M. Metzger is the executive director. The plan, which offers twenty-one days of hospital care, exclusive of physicians' fees, has been approved by the Medical Society of the County of Erie. The charter provides for service for Erie, Niagara and Chautauqua counties. Eight hospitals in Buffalo, one in Lackawanna and two in Niagara Falls are participating, each represented on the board of directors. The medical societies concerned are also represented on the board.

New York City

Birth Control Conference.—A Conference on Contraceptive Research and Clinical Practice will be held at the Hotel Roosevelt December 29-30 under the auspices of the Birth Control Clinical Research Bureau. Tuesday's program will be devoted to "Present Day Research in Conception" and Wednesday's to "Clinical Practice." Tuesday evening there will be a dinner meeting at which Dr. Ira S. Wile will be toastmaster and the speakers will be Drs. Hannah M. Stone; Milton C. Winternitz, New Haven; Mrs. Margaret Sanger, and Morris L. Ernst. The subject to be discussed is "Public Health and Birth Control Laws."

Personal.—A portrait of Mary Swartz Rose, Ph.D., professor of nutrition, Teachers College, Columbia University, was recently presented to the college by former students and associates. Dr. Rose is a member of the Council on Foods of the American Medical Association.——Dr. Thomas H. Russell has succeeded Dr. Charles Gordon Heyd, President of the American Medical Association, as executive officer of the department of surgery at New York Post-Graduate Medical School and director of the surgical service at New York Post-Graduate Hospital and Dispensary. Dr. Russell was also promoted to the rank of professor of surgery. Dr. Heyd retains his title of professor of clinical surgery.——Dr. Fred H. Albee presented a paper on "Arthroplasty of the Knee" at the meeting of the International Society of Orthopedic Surgery and Traumatology in Bologna and Rome recently and was elected vice president of the organization.——Dr. William Bierman, assistant clinical professor of therapeutics at New York University College of Medicine, was recently appointed administrative consultant in physical therapy to the department of hospitals.

Society News.—Dr. Morris Fishbein, Chicago, editor of THE JOURNAL, among others, addressed the Medical Society of the County of Kings, December 15, on "New Forms of Medical Practice."——Drs. Frederick T. Lord, Boston, and Frederic Maurice McPhedran, Philadelphia, addressed the Brooklyn Thoracic Society, December 18, on "Diagnosis of Pulmonary Tuberculosis" and "Pathology of Tuberculosis in Relation to Its Clinical Course" respectively.——Dr. Walter Schiller, Vienna, Austria, addressed the New York Pathological Society, December 17, on "Mesonephroma Ovarii."——The eighth clinical session on pulmonary diseases under the auspices of the Tuberculosis Sanatorium Conference of Metropolitan New York was held at Cornell University Medical College, December 2.——A section on medical history was recently organized in the Medical Society of the County of Kings and held its first meeting November 13, with Dr. Thomas Darlington as the speaker on "Medical Practice in Arizona in the Late Eighties."——Dr. Joseph Wrana gave an afternoon lecture before the Medical Society of the County of Queens, November 6, on "Common Diseases of the Cervix," and Dr. Moses Cohen spoke, November 20, on "Complications During Pregnancy and Their Management."

NORTH DAKOTA

Society News.—The Rolette County Medical Society was recently organized at a meeting in Rolla, with Dr. Joseph O. Hayhurst, Rolette, as president; Dr. Bernard D. Verret, Rolla, vice president, and Dr. Milton Greengard, Rolla, secretary.——

The fall meeting of the North Dakota Academy of Ophthalmology and Otolaryngology was held at Fargo, October 31; the speakers were Dr. Trygve Oftedal, Fargo, on "Tuberculin in Ophthalmology"; Clarence Wulling, Minneapolis, "Practical Optics," and Dr. George C. Foster, Fargo, "Osteomyelitis of the Facial Bones and Skull."

OHIO

Bacteriologists Organize.—An Association of Bacteriologists in Ohio was organized at a meeting in Columbus December 5, with the following officers: Dr. Noel Paul Hudson, professor of bacteriology, Ohio State University College of Medicine, Columbus, chairman; Dr. Merlin L. Cooper, assistant professor of pediatrics, University of Cincinnati College of Medicine, Cincinnati, vice chairman, and William A. Starin, Ph.D., professor of bacteriology at Ohio State, Columbus, secretary. A dinner meeting was addressed by Dr. Charles A. Doan, professor of medicine and medical research at Ohio State, on "The Place of Bacteriology in Modern Medical Science."

PENNSYLVANIA

Personal.—Dr. Thomas I. Cottom, Selinsgrove, has been appointed superintendent of the State Colony for Epileptics, Selinsgrove, to succeed Dr. Chester A. Marsh.——Dr. William M. Guilford, Lebanon, celebrated his one hundred and fourth birthday November 26.

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Pennsylvania is required by law to register annually, on or before January 1, with the board of medical education and licensure in the department of public instruction, and to pay a fee of $1 or such fee as may be fixed by the department of public instruction. A practitioner who fails to register and who continues to practice is liable to a fine of from $10 to $100.

Philadelphia

Society News.—At a meeting of the Pennsylvania Physical Therapy Association, December 10, the speakers were Drs. Albert A. Martucci, on "Experimental and Clinical Observations in Cerebral Diathermy"; Frank Follweiler, Jenkintown, Pa., "The Value of Physical Therapy in Nose, Throat and Ear Conditions," and Thomas Leichner, "Value of Short Wave Diathermy in the Treatment of Sinusitis."——A symposium on the endocrine glands was presented at a meeting of the Philadelphia County Medical Society, December 9, by Drs. Eugene M. K. Geiling, Chicago; Leonard G. Rowntree, Philadelphia, and Emil Novak, Baltimore.——Dr. Leroy U. Gardner, Saranac Lake, New York, addressed the Pathological Society of Philadelphia, December 10, on "Silicosis and Related Conditions."——Among others, Drs. Ernest A. Spiegel and Charles M. M. Gruber addressed the Physiological Society of Philadelphia, November 16, on "Subcortical Activities" and "The Cardiac Action of Thiobarbiturates" respectively.——A symposium on diseases of the respiratory tract was presented before the North End Medical Society and the North Branch of the Philadelphia County Medical Society, November 19, by Drs. George M. Coates and Hobart A. Reimann.

Pittsburgh

Personal.—Dr. Camilla M. Anderson, Pittsburgh, has been appointed secretary of the Pennsylvania Mental Hygiene Committee of the Public Charities Association to succeed Dr. Leroy M. A. Maeder, Philadelphia.

New Health Director Appointed.—Dr. I. Hope Alexander has been appointed health director of Pittsburgh, according to the *Pittsburgh Medical Bulletin*, succeeding Dr. Ray P. Moyer. Dr. Alexander was graduated from the University of Pennsylvania Department of Medicine in 1906. He is chief of the medical staff of Passavant Hospital and professor of physical diagnosis in the school of dentistry of the University of Pittsburgh. During the World War he served as chief medical officer of a government hospital in North Carolina. In 1931 he was president of the Allegheny County Medical Society. For the last three years he has been president of the Pittsburgh chapter of the Izaak Walton League of America.

TEXAS

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Texas is required by law to register annually on or before January 1, with the state board of medical examiners, and at that time to pay a fee of $2. If a practitioner fails to renew his registration within sixty days after January 1, his license is suspended.

Endowment for State Medical Library.—The *Texas State Medical Journal* announces that Dr. Samuel E. Thompson, Kerrville, has designated the library of the State Medical Association of Texas in his will to receive a bequest of about $50,000. The fund will bear the name of the giver and the principal will remain intact, the interest to be expended by the trustees to develop the library. Dr. Thompson is 65 years old, a graduate of the Kentucky School of Medicine, class of 1904. He is medical director and superintendent of the Thompson Sanatorium for tuberculosis, Kerrville, established in 1917.

VIRGINIA

Field Clinician Appointed.—Dr. Jay M. Arena, associate in pediatrics at Duke University School of Medicine, Durham, N. C., has been appointed field clinician to conduct graduate courses in pediatrics under the auspices of the department of clinical and medical education of the Medical Society of Virginia. Dr. Arena conducted a graduate course for physicians in Nelson and Orange counties, with lectures and clinics at Livingston and Orange.

Society News.—At the meeting of the Fourth District Medical Society in Hopewell, November 10, Dr. William M. Bickers, Richmond, was the guest speaker, on "Treatment of Sterility in the Female." Other speakers on the program, all of Petersburg, were Drs. Charles S. Dodd on "Ludwig's Angina"; William B. McIlwaine III, "Lung Abscess in Children"; George H. Reese, "Significance of Abdominal Pain"; Herbert C. Jones, "Urinary Infections," and Hyman Cantor, "Treatment of Compound Fractures."——Dr. Gregory Zilboorg, New York, addressed the Richmond Academy of Medicine, November 10, on "The Organic versus the Mental in Psychiatry."

WEST VIRGINIA

Headquarters Remodeled.—The headquarters of the West Virginia State Medical Association in the public library of Charleston have been remodeled. A private entrance has been cut and a new lighting system installed. The association's library and reception room have been redecorated and refurnished in modern style. The library contains about 1,200 volumes and has on file about seventy-five American and European medical journals.

PHILIPPINE ISLANDS

Plan to Improve Diet of Filipinos.—The Philippine Council of Hygiene recently appointed a committee to gather information necessary for the formulation of concrete plans for improving the diet of the Filipinos, according to the *Journal of the Philippine Islands Medical Association*. Special attention will be directed to the diet of the army and to methods of producing cheap foods. Members of the committee are Manuel Roxas, LL.B., representing the National Research Council of the Philippine Islands; Drs. Isabelo Concepcion, representing the College of Medicine, University of the Philippines; Hilario Lara, representing the Council of Hygiene, and Attorney Lara.

GENERAL

Bequests and Donations.—The following bequests and donations have recently been announced:

New York Medical College and Flower Hospital, $50,000 by the will of the late Elias C. Benedict; $5,000 by the will of the late George Leask.

Hospital for Joint Diseases, New York, $3,942 by the will of the late Charles L. Hoffmann.

Richmond Memorial Hospital, Princes Bay, Staten Island, N. Y., $35,525, and Staten Island Hospital, Tompkinsville, N. Y., $20,000 by the will of the late Frederick Keteltes.

Montefiore and Mount Sinai hospitals, New York, $8,115 each by the will of the late Henry Ollesheimer; $2,500 each by the will of Jacob W. Gutman.

News of Epidemics.—About fifty cases of smallpox were reported in Dansville, N. Y., December 9. It was said that Hornell, eighteen miles from Dansville, had seven cases.——Eight cases of typhoid were reported in Swains, N. Y., a village of 100 inhabitants with no physician, newspapers reported December 8.——Schools were to open in Tulsa, Okla., November 30, after a month's vacation because of infantile paralysis; seventy-six cases had occurred in Tulsa County up to November 20, sixty-four of them in the city.——An outbreak of scarlet fever was reported at a state penal farm at Vandalia, Ill., November 18.——Scarlet fever appeared in fourteen public schools and one private school in Dallas, Texas, with thirty-nine cases in the first three weeks of November.——Thirteen recent cases of typhoid in Cecil, Washington County, Pa., were traced to contaminated water.——Newspapers reported thirty cases of diphtheria in an epidemic at Lost Creek, Harrison County, W. Va., November 19.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 14, 1936.

Medical Coroners

At present the majority of coroners are lawyers but a minority are physicians. A committee appointed by the government to inquire into the law and practice of coroners' inquests made a report (THE JOURNAL, March 21, p. 1018) recommending that in future only lawyers should be appointed to the office of coroner, as the sifting of evidence requires legal training and a coroner without medical knowledge would be fully informed of the medical aspects of the case by the medical witnesses. The *British Medical Journal* objected to this recommendation. It admitted the desirability of the coroner having legal knowledge but thought it almost essential that he should also have medical knowledge. It pointed out that a large number of persons qualified for both professions. It has been the practice of the London County Council since 1919 to require from candidates for the position of coroner both legal and medical qualifications, but because of the recommendation of the government committee it proposes to discontinue the requirements of a dual qualification and to appoint only a lawyer. A deputation of the British Medical Association therefore submitted to the council a memorandum against this change. It pointed out that the coroners' act of 1926 enacted that no person could be appointed coroner who was not a lawyer or physician and that undoubtedly the representations of the association received due consideration when this law was passed. Since that time the association has urged the desirability of the dual qualification when practicable. All the London coroners except one hold the dual qualification and so do many of the coroners of the larger districts outside London, where they are of sufficient size to justify an appropriate salary. There has been no attack on doubly qualified coroners as such. Indeed, the inquests that attracted notoriety in the press and gave rise to the appointment of the government committee were conducted by coroners holding only legal qualifications. The report recommends that a "coroner should have training in forensic medicine." This is a cogent reason for appointing doubly qualified men. The association "cannot conceive how the possession of two qualifications—law and medicine—could be considered less desirable than one qualification—law—with only a smattering of forensic medicine." There is at present no dearth of doubly qualified suitable men for any appointment that may become vacant.

The importance of legal knowledge by the coroner has been reduced by recent legislation. Since 1927 he has been required to adjourn his inquiry after hearing the medical evidence when any person has been charged with murder, manslaughter or infanticide. Moreover, the committee recommended that his investigation of fact should be clearly distinguished from any trial or liability, whether civil or criminal. On the other hand, the medical aspect of the coroner's work is becoming more important. In London in 1934, 9,713 cases were reported to the coroner either through the police or through the physician who felt that he was not justified in taking the responsibility of issuing a death certificate, or by the registrar of deaths who did not feel justified in passing a certificate for registration. These cases are divided into those in which a coroner is compelled to hold an inquest and those in which, after a necropsy and inquiry, he can exercise discretion and on his own responsibility issue a certificate without an inquest. In London in 1934, 52 per cent of the cases referred to all the coroners were dealt with without an inquest and as a result of a necropsy. Altogether in 1934 there were 6,248 necropsies. How does a legal coroner read a report of a necropsy? However much he may have read textbooks he will never do so with the seeing eye of the physician.

Street Washing for Removing Poison Gas

This country, which once could rely for its safety on sea power, is now actively engaged in measures for defense against attack from the air, a possibility that cannot be ignored in the present disturbed international relations in Europe. The latest precaution is shown by a demonstration at Watford of the new Scammel street washer, which is effectual not only in fighting fires but in freeing the streets from poison gas after air raids. Out of the old fashioned watering cart has been evolved this highly efficient machine. It can spray water over a width of 90 feet and is capable of sending an arc of spray to reach the roof of a two story house. Streets where poison gas was present after an air raid would first be washed in this way and then under low pressure. At the same time the squeegees with which the washer is equipped would be brought into use for cleaning and to some extent for drying the road surface. The third stage of the decontamination of the streets would be to flush chemicals through the gullies. This would normally be done by connecting the nearest hydrant, but where the water main had been broken in an air raid the machine could do the work with its own power.

To aid the dispersal of nonpersistent gases the machine has a special piece of equipment in the shape of four "fishtails," which can take the place of the ordinary washing jets and which are mounted on ball joints to give freer movement. When these are set in motion they produce a fan-shaped sheet of water, which completely encircles the vehicle to a height of 30 feet and a width of 70 feet. Such a device makes it possible to purify the air and to wash the roofs of buildings and the sides of vehicles that have been contaminated.

An Earlier "British Medical Journal"?

It is generally supposed that the title "British Medical Journal" was first used in 1857 for a journal previously in existence for seventeen years which bore the name first of *Provincial Medical and Surgical Journal* and then of the *Association Medical Journal*. But *nil novum sub sole*. Our contemporary has discovered that the title "British Medical Journal" was announced for a new periodical at the end of the eighteenth century, though whether it ever appeared seems more than doubtful. A printed prospectus in the form of a four page leaflet was issued in London in 1798 and begins thus: "On the 1st of February, 1799, will be published, price two shillings, elegantly printed on fine Demy Paper, octavo size, containing at least six sheets of letterpress and embellished with one or two plates, to be continued monthly, Number 1 of a New, Useful and interesting Periodical Work, intitled the *British Medical Journal;* containing the Earliest Information on Subjects of Medicine, Surgery, Chemistry, Pharmacy, Botany and Natural History." The prospectus is lengthy and gives under ten headings everything that a medical journal could be expected to do—recent improvement and discovery in botany, chemistry, pharmacy and other medical sciences, an abridged view of the prevailing epidemics, "impartial histories of the most celebrated patent and other quack medicines," remarkable and authentic medical cases, descriptions of countries and places as to their salubrity, a review of all new publications in the various departments of medical science, and monthly tables of the variations in the wholesale price of drugs. One reads: "There is at present no monthly journal in the English language the professed and single design of which is to communicate accounts of every new observation and valuable discovery made from time to time in the different branches of medicine. An early circulation of intelligence so essential to the practitioner, as well as to society in general, has not been

attended to with the care which the importance of the object required." Though written nearly 150 years ago, when medical science was so different, this prospectus has a familiar ring. It reminds us of the lofty aims and the wants that have never been filled before, or at least so well filled as they will be, by some new journal about to be or just launched. The subsequent failure to realize high hopes is also not without more recent parallels. But we have advanced in one way. Such prolixity would not be possible in an editorial announcement today, though the same could not be said of the ordinary medical article.

The Training of Factory Nurses

The increased attention to industrial welfare has led to the appointing of physicians and nurses to factories. But it is not every factory that can afford to employ both, and a nurse who works alone has considerable responsibility. Her work consists not only in the treatment of accidents and minor injuries but in advice as to health. In the case of processes involving special risk or strain she may have to carry out special treatment under medical supervision. She therefore requires special training. For the past two years the College of Nursing has provided special courses of instruction for nurses who undertake factory work.

PARIS

(From Our Regular Correspondent)

Nov. 21, 1936.

The Surgical Congress

In THE JOURNAL, November 14, page 1647, the reports read at this year's French Surgical Congress were referred to. In addition to the participants previously cited, the subject of ovarian grafts was discussed by other speakers. Mayer of Brussels disagreed with the reporters in saying that intramuscular grafts were not successful in female dogs. His own experiments showed that such was not the case and that if the grafts did not survive it was due to a faulty technic. He prefers instead of placing the graft clinically in the abdomen to insert it into either the rectus (abdominal) muscles or the subcutaneous or retromammary connective tissue. In cases in which the uterus had been conserved, the ovarian grafts were successful in 88 per cent of the cases. Menstruation recurred regularly for several years. In supravaginal hysterectomy cases he could cite only 50 per cent successes.

Desmarest of Paris emphasized the necessity of conservation of the tubes and ovaries in cases of hysterectomy for fibroids. Eighty per cent of his patients had no disturbances following such a procedure. The estrogen content of the urine in such patients is equal to that of women having normal menstruation. This is also true of the estrogen content of the blood. In uterine fibroids, if myomectomy is impossible, only a supravaginal hysterectomy with conservation of the tubes and ovaries is indicated.

The discussion on the subject of pneumonectomy was continued by Rist of Paris, who stated that the present tendency of regarding bronchiectasis as a benign disturbance is too prevalent. Bronchiectasis always ends fatally, after a prolonged clinical course. If, however, bronchiectasis is treated during an early period of its development, a thoracoplasty, with in some cases also a phrenicectomy, can be of great benefit.

Among other papers read was one on foreign bodies in the esophagus, by Jean Guisez of Paris, who has observed 530 cases. The most frequent foreign bodies (200 cases) that lodge in the upper portion of the esophagus are small bones (especially those of fishes). In seventy-two patients a set of false teeth had been swallowed, and next in frequency were buttons, open safety pins and coins in infants. He had removed, with the aid of esophagoscopy, an open safety pin from a 6 weeks old child. The most reliable clinical symptom of foreign bodies in the esophagus is complete inability to swallow either liquids or solids. At times there is a complete absence of any clinical signs in children who have swallowed metallic bodies, because these are well tolerated. This is not true of small bones, the lodgment of which is apt to be followed by septic complications either in or outside the esophagus. Endoscopy has greatly facilitated the removal of foreign bodies in the esophagus. His mortality in 530 cases was only 2 per cent, and he was unable to deliver the foreign body in only 1 per cent. In the last 220 cases he had only one death and no failures of extraction. The death occurred in an adult whose false teeth had lodged so firmly in the upper part of the esophagus that several attempts had been unsuccessful before the patient was seen by Guisez.

Ferey of Saint Malo (France) reported eighty-two cesarean operations performed during the past six years. Of these, seventy-six were of the low type, one of the high and five a section followed by hysterectomy. He has performed the low cesarean operation in eighty-eight cases without a death and believes that this technic has innumerable advantages over the high operation.

Judet of Paris has been obliged to operate only once in 300 cases of supracondyloid fractures of the humerus in children. If the reduction can be made under fluoroscopic control within a few hours after the accident, complete approximation of fragments is always possible. The elbow should never be placed in extreme flexion because of the danger of interference with the blood supply (brachial artery) and resultant Volkmann contracture. Operation is indicated only if nerve or vascular complications exist.

Familial Intolerance of Mercury by the Kidneys

At the June 19 meeting of the Société médicale des hôpitaux, Tzanck and associates reported two cases in the same family of intolerance of mercury by the kidneys. A man, aged 44, received injections of mercuric oxycyanide for hereditary syphilis. Two hours after the first injection, the previously existing headache became more severe and the next day an edema involving both lower extremities and a very marked albuminuria appeared. Following a second injection the patient became comatose. The injections were discontinued and all symptoms disappeared in a few days. Since then a bismuth treatment has been given without any further signs of renal intolerance. The daughter of the patient showed evidences of hereditary syphilis. Following a series of mercury inunctions when she was 5 months old, a hematuria appeared. This recurred when an ointment containing yellow mercuric oxide was given at the age of 4 years. Thus there were two members of the same family who manifested a renal intolerance to mercury.

Experimental Syndrome Resembling Obliterating Thrombangitis

At the July 1 meeting of the Académie de chirurgie, Leriche and Froehlich described experiments on rabbits, like those of Maggi and Mazzochi, reported in 1933, in which lesions like those observed in obliterating thrombangitis were observed after transplantations of fragments of the adrenal. This was done every four days by Leriche and Froehlich. In the controls, in which testicular and ovarian grafts were used, the veins and arteries remained intact. In all the rabbits in which fragments of the adrenal were transplanted, both arterial and venous lesions appeared which resembled greatly those seen in human beings. The lesions were slight when only six to ten grafts were used but very marked when twenty or more were employed. The chief changes observed were considerable narrowing of the arterial lumen, general contraction of the vessel, proliferation of the endothelium, which is very thick in places, with increase in the elastic fibers, the latter two changes forming marked salients into the lumen. At this point, a thrombus

formed, and one could see a sclerotic tissue replacing the muscular fibers. In certain veins the same changes excepting the thrombus formation were visible. In a rabbit that had received thirty-nine grafts and been kept under observation for a little over six months, the femoral artery was found to be completely occluded and a persistent ulcer appeared on one of the paws. Fontaine had previously noted similar thromboses of veins and arteries following daily injections of cholesterin over a period of six months. If one recalls that the medullary portion of the adrenal plays a fundamental part in the metabolism of the cholesterols, it seems probable that thrombangitis with arterial and venous lesions is the clinical expression of an adrenal disease. This agrees with the results obtained by Leriche by removal of the adrenal or division of the splanchnics, which partially denervates the adrenal.

The Organization of Health Centers

The medical profession, through its Federation of Medical Syndicates or Unions, has proposed to the secretary of public health to take charge of his plan of organizing health centers all over France. The object of the federation is to keep this feature of social medicine in the hands of the practitioner instead of permitting it to be administered by officials of the department of public health. There has, of course, arisen some opposition within the ranks of the profession, but this has been overcome, since it is evident that, unless the present socialist government is given cooperation in its program, the alternative will be state medicine and the disappearance of private practice.

In the October 4 *Concours médical* appeared an impartial discussion by Dr. Fischer of such cooperation, stating that, considering the rapidity of social revolutions, this offer of cooperation is the only way of safeguarding traditional medicine and conciliating its needs with the requirements of hygiene and prophylaxis that those who wish to socialize medicine demand to protect the public.

The manner in which social insurance was forced on the profession has compelled physicians, especially the younger ones, to adapt themselves to new conditions which were formerly rejected. Fischer believes that the assumption of the task of preventive medicine should be carefully worked out lest failure to carry it out properly be followed by worse conditions than exist at present. The medical profession, having had its experience with the manner in which many promises were not kept by the social insurance authorities, should present a united front on the present question of cooperation in preventive medicine.

The plan is not to be tried out in large communities like Paris, which present complicated problems, but in a smaller department or county to begin with. The majority of the work can be carried out in the offices of practitioners. It is to be only of a diagnostic nature, so that the patient can still choose the physician he wishes to carry out the treatment. A committee of coordination composed of physicians and public officials ought to meet every three months to supervise the work. In larger communities it is planned to have diagnostic centers fully equipped with all modern diagnostic resources. This plan of cooperation is soon to be submitted to the secretary of public health.

Protest Against Foreign Physicians in France

A want ad for a position as medical inspector in the social insurance organization recently appeared in the *Concours médical* and there were eight applicants for the position. In an editorial appearing in the September 19 issue of the journal the writer, Dr. J. Noir, asks whether this relatively large number of applicants for such a position does not signify that many middle-aged physicians are seeking a haven in which they would no longer have any worries regarding their income. The advertisement stated that only those need apply who had been in practice at least ten years. This would exclude as applicants recent graduates who had not yet built up a practice. The rôle of foreign-born physicians practicing in France, as revealed by Dr. Queyrrious at a meeting of the syndicate of physicians in the northern suburbs of Paris, is quoted in the editorial. More than one fourth of the practitioners in Paris and its suburbs are non-naturalized foreigners. This percentage was only 8 in 1911 and 10 in 1931. Fifteen per cent of the physicians in all France were foreigners in 1935. At the Faculté de médecine, the largest medical school in France, there were 1,530 foreigners out of a total of 3,332 students; 689 of the 1,530 foreign students were preparing to pass the examinations for licenses to practice in France and the remainder wished only to have an honorary "diplôme d'état," which does not entitle them to practice in France or its colonies unless they pass additional examinations, which some of them will probably try to do. During the first six months of 1936, 163 foreign physicians registered their state licenses in Paris, as compared with 124 of French birth. The present socialist prime minister is quoted as having stated that about a thousand physicians who have sought refuge in France will be granted permission to practice here. An effort is being made by the various medical syndicates (associations to protect the interests of the profession) to insist on the enforcement of a law which will prevent any foreign-born physician practicing in France and its colonies during a period of ten years after naturalization. Noir regards the invasion of the profession by foreign physicians as the most important factor in the present medical crisis here.

University Diploma Falsely Registered

There is quite a sharp distinction in France between a university diploma of a medical school and the state diploma, which alone confers the right to practice. Following the passage of the new license laws in 1933, every diploma was verified by representatives of the government and of the medical profession.

A foreigner, who had passed only the examinations required in order to obtain a university diploma, had succeeded in having it registered by the police department (where all diplomas must be registered) as a state diploma, conferring the right to practice. Many foreigners, especially since the World War, have entered medical schools in France and followed the courses leading to the university diploma. The latter is often of considerable value in the foreigner's native country in obtaining the state license. At one time there were a number of North and South American and European medical students who had not been eligible to admission to schools at home and expected their studies in French universities to serve as credits toward obtaining a state license at home. This practice has been entirely abandoned in most European countries, with the result that the number of candidates for a university diploma has greatly diminished here.

The possessor of the university diploma, in the case cited, refused to discontinue practice, on the ground that his diploma had been duly registered, although the registration had been done by a clerk who did not realize the difference between a university and a state diploma. To obtain the state diploma, the student not only must pass all the examinations at the respective medical school, as is required also of the candidate for a university diploma, but must have received the bachelor of arts degree from a French university. The latter requirement has been the chief stumbling block in the past for American physicians who wished to practice here. According to the present laws (since 1933) only those foreigners who were practicing in France and had a state license could continue to do so.

The government authorities have just decided that the physician who had only a university diploma and had it registered as a state diploma was not entitled to practice here. This decision will put an end to any attempts by foreigners, who

have flocked to France in large numbers recently, to utilize their university diplomas, which are of purely honorary character, to remain here.

Plea for a Single Medical Diploma

As explained previously, a medical student in France can elect to graduate with a university diploma (diplôme universitaire), a purely honorary one, which does not entitle its holder to practice in France or its colonies, or to graduate with a state diploma (diplôme d'état), which carries with it the right to practice without the obligation to pass any other examinations than those given by the faculty of the medical school. The only difference between these two forms of diplomas in France is that the candidate for a state diploma must have received a bachelor of arts degree from a French university. Those granted by universities of other countries are not considered valid here. Many protests are being made against this dual system and sooner or later it will be discarded in favor of a single diploma to be followed by a state board examination for all candidates, as now exists in the United States, Germany and other countries. A writer in the *Revue moderne de médecine et chirurgie,* Dr. P. Gallois, makes a strong plea for the granting of only one type of diploma and a subsequent state board examination. Such a licensing board should have full power to refuse permission to practice to those who are not French citizens, possess a bachelor of arts degree, have had three years' military service and have been naturalized a minimum of ten years. Only in this way can the overcrowding of the profession here by foreigners during recent years be checked. This would put a stop to the present method so often employed by foreigners of changing a university to a state diploma by simply passing the examinations for the bachelor of arts degree at a later date.

"Mock" Night Attack of Enemy Bombers

For the first time since the World War, Paris extinguished its myriad lights and shrouded itself in darkness, October 16, in defense against an air attack. While supposed enemy bombing planes circled over the obscured city, dropping flares representing destructive explosives and poisonous gases, fire engines sped through the dark streets to combat "fires," and ambulances rushed the "gassed and injured" to first aid stations. All traffic was halted, and automobiles and other conveyances remained motionless while the hypothetical attack was in progress. Notice of the impending attack was given by the screeching of seventy sirens. The center of the sham air raid was in the Latin quarter. Red Cross nurses and stretcher bearers protected by gas masks picked up the wounded and transported them to hospitals, while disinfecting squads purified the air. Observation planes passed overhead to measure the extent to which the city had become invisible. Experts declared that the actual tests worked out with minute precision, and relief squads operated efficiently throughout the city.

Transfusion of Refrigerated Citrated Blood

Reference has already been made in these letters to the success in using blood for transfusion which has been placed in a refrigerator, following dilution with sodium citrate. Professor Jeanneney of Bordeaux was the first to suggest this method of conserving blood, which has been extensively employed in southwestern France and in Russia. In the latter country, Bagdassaroff of Moscow has employed this method 2,400 times, and Filatoff and Bopp of Petrograd 1,200 times.

Tullien-Neroz, a pupil of Jeanneney, in a thesis submitted for graduation in 1935, called attention to the manifold advantakes of the conserved blood method. The practitioner has at his disposal ready for use blood that has been strictly controlled in advance as to grouping and the presence of such diseases as syphilis and malaria in the donor. Such blood is also immediately available for the purpose of immunotransfusion. The blood as soon as received from the donor is mixed in a 250 cc. flask containing 20 cc. of a 5 per cent solution of sodium citrate. A tag on the flask indicates the name of the donor, the group and the date on which the blood was taken. The flask is then placed in a refrigerator at a temperature of 2 C. (35.6 F.). The blood is available for immediate use during a period of eighteen days and even longer. The changes undergone by the refrigerated blood are of no importance clinically. The method avoids having donors on call and has the advantage of being available in emergency cases.

International Congress of Physical Education in 1937

At the Paris Exposition of 1937, an International Congress of Physical Education and Sport will be held during the week beginning July 14. The National Committee of French Sports and the president of the committee of organization, Dr. Collect, will have charge of the program. The object of the congress is to interest the French medical profession in encouraging boys and girls to take up sports in a more active manner than is at present the case. Intercollegiate competition is but little developed here, in spite of the fact that an assistant secretary of sports position in the cabinet has existed for some time.

Souvenirs of the Charité Hospital

Reference has been made in these letters to the demolition of the historic Charité Hospital in Paris in order to provide space for the new laboratory buildings of the medical school. The salles de garde of the older Paris hospitals are of great interest to those interested in medical history. The salle de garde of the Charité, or room in which the interns on duty for emergency cases assembled, sheltered during its 300 years of existence many of the most famous medical men of France during their internship at the Charité. On the walls of this particular salle de garde were a number of paintings by the best French artists of the respective periods. One of the most interesting of these paintings shows Velpeau and his intern chasing a quack, who even in those days guaranteed to cure cancer, from the Temple of Science. As a result of the initiative of Dr. Mourier, director of the public hospitals of Paris, all these paintings, which will be of great value to those interested in medical history, have been placed in a museum on the de la Tournelle in the center of Paris.

Laignel-Levastine Elected to Academy

Election as a fellow of the Académie de médecine is considered one of the highest honors that can be conferred on a member of the profession. At a recent meeting of the Académie, Dr. Laignel-Levastine of the Hôpital Lariboisière, neurologist and medical historian, was elected. He is professor of the history of medicine at the medical school of the University of Paris and secretary of the International Society of the History of Medicine.

Death of Dr. Jean Charcot

The sad death of Dr. Jean Charcot, captain of the vessel *Pourquoi Pas,* and all the crew except one, by shipwreck on the coast of Iceland during his last scientific expedition, was reported a few weeks ago in the daily papers. Jean Charcot was the son of the late Prof. Jean-Martin Charcot, the internationally known neurologist of the Salpêtrière, and was born in Paris in 1867. Following an internship in the Paris hospitals, he became chief of clinic at the Salpêtrière but soon ceased to practice and began his first oceanographic expeditions. He was especially interested in the study of geographic conditions at the north pole and in 1912 was given the grand medal of the French Geographic Society. After the World War he organized another expedition and brought back a large number

of important observations. As a recognition of his contributions to science he was elected a fellow of the Academy of Science and Academy of Medicine. Following the death of Dr. Charcot and his companions on his last polar expedition, the French government has decided to pay the highest honors in the form of a national funeral to the dead heroes as soon as the remains arrive in Paris. A special medal to commemorate the work of Dr. Charcot has also been ordered.

BERLIN

(From Our Regular Correspondent)

Oct. 26, 1936.

International Congress of Otorhinolaryngologists

The third International Congress of Otorhinolaryngologists was held at Berlin in August. Professor von Eicken presided. About 800 delegates, German and foreign, participated.

The first speaker, on the topic "Radiotherapy in Malignant Tumor Cases," was Berven of Stockholm, who is accustomed to treat malignant tumors of the oral cavity and of the mesopharynx with radium and, much less frequently, with roentgen rays. Because of the relatively large supply of radium available at the Stockholm "Radium Home" it is possible to administer teleradium therapy by means of "radium guns" which contain from 3 to 8 Gm. of radium sulfate. This offers the widest range of possible approaches as, for example, multiple field irradiation and cross-fire irradiation. Daily and total dosage are adapted to the requirements of each case; in addition, the general condition and age of the patient, and the best type of adjuvant treatment to be introduced are all considerations. The Stockholm men have also worked out a therapeutic program under which early stage syphilis cases have decreased from 60 per cent to 35 per cent within a ten year period. Late stage syphilis, on the contrary, has increased from 40 per cent to 60 per cent during the same period. This shows how rapidly and successfully the early stage cases are being combated. Naturally the excellent organization of the Stockholm institution has contributed to these favorable results.

Hautant of Paris undertook, in collaboration with Coutard, the treatment of cancer of the larynx at the Curie Institute, Paris; 25 per cent of 122 such cases could be considered cured at the end of a nine year follow up. Choice of irradiation or of operative treatment was made on the basis of the situation and type of the cancer and the patient's general condition. Irradiation is usually indicated if infiltration has not yet begun. If the vocal chords are still movable, it may be assumed that the carcinoma is not yet infiltrating. Otherwise the efficacy of the roentgen rays is dubious. According to Hautant's experiments "the epidermal epitheliomas, exophytic and vegetative in form," the cells of which have undergone only a suggestion of epidermoid alteration or none whatever, may be effectively irradiated. Other carcinomas of the infiltrating, ulcerating type are refractive to the rays, particularly if horny pearls are present in the altered epidermoid tissue.

Maisin of Louvain obtained his optimal results if the malignant growth had its seat in a tonsil or the distal two thirds of the tongue. Contrary to expectations, a combination of surgical therapy and radiotherapy yielded rather unfavorable results in the treatment of metastases in the lymphatics. Here roentgen treatment alone seemed to be advisable. Teleradium therapy appears most favorable if a cartridge containing 7 Gm. of radium is used.

Torrigiani of Florence applies protracted fractionated irradiation in cancer of the larynx and also in treating the lymph nodes. In cases of tumors within the accessory nasal cavities he recommends radiosurgery: a wide opening should be effected through the healthy palate in order that the region of the tumor may be treated by the most delicate technical procedures and any recurrence may be detected. If a malignant tumor is situated in the ethmoid bone, an eye must be sacrificed if necessary in order that the focus may be more directly approached.

Schinz of Zurich determined by a vast amount of experimentation that better results were obtainable with the protracted-fractionated method of irradiation. To be sure, the sum of the end results of irradiation is not yet numerically as impressive as the sum of the results of operative treatment, but one must remember that the data on operative treatment have to do exclusively with more favorable cases.

Vogel of the Berlin clinic discussed the curative treatment of carcinoma of the vocal chords by a combination of operation and irradiation (thyroid cartilage fenestration) which, he said, is effective in an average of 90 per cent of such cases. In a large proportion of the cases, permanent cure has been determined by follow up of from five to seven years' duration. In 40 per cent of other cancers, likewise situated within the larynx, cure was effected by protracted fractionated roentgen irradiation and without surgical intervention; here, too, numerous cases exhibited no signs of recurrence after the lapse of more than three years.

The second major topic was "Electro-Acoustic Apparatus for the Testing and Improvement of Hearing." Langenbeck of Leipzig spoke of the advances made within the last twenty years through electro-acoustics. Electrical testing of hearing with the audiometer belongs today among the indispensable tools of clinical diagnostics. In the realm of auditory prosthesis, development as far as medical research is concerned is now essentially a question of technic. In this connection Pohlman of Omaha demonstrated a simple yet obviously effective hearing prosthesis. The theory of this device proceeds from anatomic assumptions. This prosthesis is soon to be examined at the Berlin clinic.

The third topic was "The Influence of the Constitution on Disorders of the Ear, Nose and Throat." It would seem that constitutional factors play a part in the manifestation of carcinoma in the hypopharynx and esophageal orifice of females.

German Institute of Psychotherapy

The German Institute of Psychologic Research and Psychotherapy (Deutsches Institut für psychologische Forschung und Psychotherapie) has been established with the sponsorship of the National Ministry of the Interior. The membership is composed of representatives of the Pan-German Society of Psychotherapy, the German Psychoanalytic Society, the Künkel cooperative group for "Applied Study of Character" and also other well known psychotherapeutists. The three last named organizations will function within the institute as cooperative societies. The duties of the institute shall be (1) research, (2) educational and teaching activities and (3) maintenance of a policlinic for the indigent. The institute begins its work with the winter semester 1936-1937. The director of the institute is Prof. Dr. M. G. Göring, president of the Pan-German Medical Society of General Psychotherapy.

Blood Tests for Alcohol in Traffic Accidents

The minister of the interior recently ordered blood tests for alcohol in connection with traffic accident cases. Such blood tests were first experimentally performed under the auspices of the Berlin police administration. On the basis of these experiments it is now stipulated that examination be made of all those persons involved in traffic accidents who are reasonably suspected of being under the influence of alcohol.

For determination of alcohol in the blood the micromethod of Widmark is indicated as a well known and reliable procedure. As soon as possible following the accident the specimen is drawn from the ear lobe or finger tip and collected in specially prepared glass tubes. The Widmark method has received recognition in an amendment to the criminal procedure

statute. In order to save expense the withdrawal of the blood specimen and the clinical examination are considered a part of the duties of the regular police physician. In order that the greatest possible exactitude and certainty may be obtained in the medical establishment of sobriety or inebriation, a medical examination must in each case be carried out and the observations properly recorded on questionnaire blanks. This procedure is particularly important if the alcoholic content of a suspected person's blood is not great enough to establish an alcoholic influence in the absence of other evidence. An especially valuable feature of the Widmark method is that by it not only the influence of alcohol but a state of sobriety may be determined; this may have a decisive bearing on the release from custody of a suspected person. Since the alcoholic content may be preserved for several weeks in the specially prepared glass tubes, the possibility of a later central examination in the main laboratory of the government hospital is guaranteed the police officials.

Marriage Prospects of Professional Men

Wissen und Dienst, the publication of the German student bodies, has taken up the problem of marriage prospects for young professional men. It was stated as an established fact that university trained men have "the fewest children of any group of the population." The causes of this circumstance are being investigated particularly with reference to the situation, peculiar to the present, which has been created by the requirements of the labor service and of the two-year military service. After four years of elementary school and nine years of secondary school, the average "prep" graduate will be 19 years old. Then after fulfilment of labor and military service he enters the university at the age of from 21 to 22. If his professional course is considered as requiring a minimum period of from four to six years (medical students must complete at least eleven semesters of study), the average age of candidates for the final academic examinations will be from 26 to 27 years. All prospective physicians, jurists, government officials and so on are compelled to put in a further period of preparatory service, which may be as long as three and a half years and during which at best only a minimal compensation is received. At the time of his entry on a regular professional career the man is thus generally from 29 to 30 years old, and even then his annual income is scarcely sufficient to support a family. The minister of the interior, seeking to remedy this deplorable state of affairs, recently announced that henceforward the usual thirteen year period of general extensive education, four years of elementary and nine years of secondary school (gymnasium), shall be reduced to a twelve year period.

Short Wave Therapy in Gynecology

Prof. Heinrich Guthmann, assistant at the university gynecologic clinic at Frankfort, recently addressed the medical society of that city. He prefaced his remarks by an objection to the term "ultrashort waves." In actual practice, radiations the wavelengths of which may vary from 3 to 15 meters are administered. Only partially understood are such biologic effects as displacement of the hydrogen ion concentration toward acidity, stimulation of phagocytosis, increase in the capillary permeability, the weakening of bacterial toxins and the reactive increase of calcium in the tissue. The complete picture corresponds to that presented by an increase in the tonus of the vagus. Because of these biologic alterations and of the active hyperemia produced by the penetrating irradiation, the procedure is applicable in all disorders in which these alterations are the desiderata and above all in inflammatory processes. In practice the local treatment, the artificial production of fever and the treatment of the superordinated organ are differentiated. In general it has been demonstrated that, in contrast to diathermy, results are favorable, the fresher the processes. Furunculosis, bartholinitis, perimetritis and adnexitis are all well influenced and favorable effects in gonorrhea have been noted. Gonorrhea of the mucosa is apparently not influenced. In genital tuberculosis this type of treatment is better endured than any other heat therapy, according to experimentation at the Frankfort gynecologic clinic. Only in those carcinoma cases in which fever was present was the treatment administered. The ill effects reported from other sources was not observed; on the contrary, there was an alleviation of pain. Neuralgias and spasms of various types react well. This treatment is indicated in inflammations of the gallbladder during pregnancy, in gonorrheal arthritis and in arthritis ovaripriva. In the last named disorder it should be combined with the administration of estrogenic preparations. The favorable results have not yet been given statistical representation. Favorable effects on the diseases have, however, been observed and the period of treatment has been shortened. Likewise of particular note are the successes achieved in cases which hitherto have been futilely treated by other methods. The treatment is seldom contraindicated. As to the method employed, the dosage in the absence of a physical measuring standard still depends in the last analysis on the thermic sensations of the patient. Individualization and consideration of the possible formation of an abscess may likewise determine the dosage and it should be assumed as axiomatic that the fresher the process the smaller the dosage to be introduced at the beginning. The method of administration will also vary according to the circumstances of a case; it depends not so much on the attainment of a maximal temperature as on the stimulation of a defense reaction in the organism. As Guthmann emphasized in his closing remarks, short wave therapy is to be regarded as a valuable physical therapeutic development. The technic must now patiently be brought to perfection.

New Procedures in Ophthalmology

Professor Jess of Leipzig recently discussed in the medical society of that place innovations in therapeutic procedure. In 1929 Heine of Kiel described the adhesive glasses which he had brought to perfection and which were to be worn beneath the eyelids for the correction of anomalies of the corneal cone and of refraction. Meanwhile Professor Jess, first at his Giessen clinic and later at Leipzig, has been able to correct a greater number of cases of the same nature also by means of the adhesive glasses. His experiments established that a distinct correction is possible but that not all patients are adaptive to the wearing of the glasses. Hypersensitive persons with prominent eyes and tense lids do not become accustomed to the device. Other persons are wont, after appropriate instruction and a period of adaptation, to become entirely reconciled to the adhesive glasses. Irritations occasionally encountered never assume a serious character; slight opacities of the corneal epithelium tend to correct themselves after a longer wearing of the glasses. Artists, sportsmen and others who shy at the wearing of spectacles are amply recompensed by a trial of these adhesive glasses.

Jess discussed among other new operative procedures the lacrimal sac operation of Toti, by which the tear flow is restored. Only in the most extreme cases should the lacrimal sacs be radically removed; namely, if the presence of a corneal tumor demands that the source of infection be immediately shut off. In all other cases the attempt should be made to render the lacrimal sac again capable of function by a wide communication with the nose. The therapeutic effects of this last named intervention are excellent but rarely is there any later coalescence and then usually only if the postoperative cure is inadequate or faulty.

The new Elschnig method of extraction of cataract in the capsule and of the removal of a luxated lens by electrocoagu-

lation is an advance over the older procedures, as in the latter, after the tearing open of the capsule, the content of the capsule sac was more or less completely removed and extensive formations of secondary cataract often took place necessitating further operative interventions. Jess therefore resorts to the older methods only in overmature and soft cataracts in which the lens normally cannot be enucleated with the capsule. For all not wholly mature cataracts in which the capsule still possesses a greater solidity, intracapsular operation is preferable and the same is true in cases requiring extraction of a luxated lens. Following excision of the cataract, the lens, which has become firmly attached to a needle electrode by electrocoagulation, may be easily removed from the eye, a procedure that formerly was possible with the aid of loops and forceps.

ITALY

(From Our Regular Correspondent)

Oct. 15, 1936.

Light as a Cause of Disease

Prof. Guido Guerrini, head of the pathologic institute of Bologna University, in a recent lecture to the army physicians spoke on light as a factor causing disease. Light is a stream of radiating waves varying in length from 4,000 angstrom units for the violet to 8,000 for the red. The action of light may be direct or indirect. Direct action induces local phenomena such as hyperemia. Indirect action induces general phenomena. The action of light depends on individual physiology, constitution, age and sex. Blond persons are forty times more sensitive to light than persons with a dark complexion. The elder are more sensitive than children and the latter more than youth. Men are twenty times more sensitive to light than women. The sensitivity of women increases during pregnancy and menstruation. The clinical forms of light disease may be phototraumatic, photodynamic, photobiologic and photo-anaphylactic. In phototraumatic light disease, the skin struck by light reflects a part but not all of the radiations. The remaining part enters the tissues. Through stimulation of the cutaneous nervous ends, hyperemia, xeroderma, senile keratosis and epitheliomatosis are induced and local inflammation results from the mobilization of histamine from the skin into the tissues and from nutritional alterations of the tissues. Light induces an accumulation of cholesterol in the uncovered surface of the skin, which facilitates metaplasia. Photodynamic light diseases are those in which light acts through catalyzing agents. The mechanism of production of photodynamic phenomena are not yet clear. Robuschi showed recently by experiments that light filtered through solutions of methyl violet kills mice, guinea-pigs and rabbits. Robuschi's phenomenon is important. Many researchers on this field have concluded that photocatalyzing agents have an inhibitive action. According to the speaker the action depends on the quantity: Large doses of photocatalyzing substances have an inhibitive action whereas small doses have a stimulative action. There are endogenous and exogenous photocatalyzing substances. The bile pigments and hematoporphyrin are endogenous photocatalyzing substances. Eosin, methylene blue, neutral red and the salts of quinine are exogenous. Pellagra, according to modern conceptions, is considered a photodynamic light disease resulting from endogenous photocatalyzing substances (indolethylamine, phenylalamine and, perhaps, hematoporphyrin) rather than from the eating of maize. Photobiotrophic light diseases are those in which light plays a part, either by stimulating specifically the action of a virus or by inhibiting the defensive resistance of the body. Spring furunculosis and staphylococcic impetigo (in which light increases the virulence of staphylococcus) as well as lichen and psoriasis are forms of photobiotrophic light diseases. In actino-anaphylactic light diseases light renders the body either more sensitive to a bacterial protein or more liberal in producing new antigens. Solar urticaria frequently has the character of a papulous dermatitis in which histamine is probably the antigen.

Vaccines and Serums for Africa

The Istituto Sieri-Vaccinogeni of Asmara is concerned with the preparation and distribution of serums and vaccines. From July 1, 1935, to April 30, 1936, 453,067 doses of smallpox vaccine were distributed in Africa. At present, 50,000 doses of the vaccine are weekly sent by air service to African sanitation centers; 44,276 head of cattle were vaccinated against plague in a month. Mortality from the plague is now 0.96 per cent. The laboratories of the institute are located several kilometers from Asmara. The institute has 3,000 heads of well fed cattle grazing. To increase the work of preventive immunization and also for making compulsory vaccination in African children, laboratories for the production of smallpox and antirabic vaccines are established at Addis Ababa. Some natives know about the benefits of vaccination and when Italian troops occupied the country they brought presents to the Italians asking to exchange them for the administration of smallpox vaccine.

Laws to Encourage Large Families

Regulations were recently approved by the council of ministers to provide married couples who have children more opportunities than couples without children. Couples will be given prizes by the provincial and the municipal authorities for having children. There will be a special prize from the state for mothers bearing twins. Parents having eight or more children are to be excluded from the payment of school taxes. Certain special licenses, which were previously necessary for the marriage of soldiers, municipal workers and women working in psychiatric institutions, have been abolished.

International Dermatologic Exhibit

Professor Tommasi, head of the syphilis and skin clinic of the University of Palermo, introduced a motion to the ninth International Congress of Dermatology which resulted in the establishment of a central office for study and interchange of scientific material. The office is called the "Centrum Commutatorium Dermatologicum," with headquarters during five years at the Budapest clinic. The work of the office will include the compilation of collections of scientific material, unification of scientific nomenclature and the teaching of dermatology. Collections will be made of photographs, microscopic slides, paraffin inclusions, wax preparations and similar material prepared in relation to rare diseases and those recently discovered and will be exhibited at the central office and its branches by changing the collections in the different branches for spreading the knowledge in different places.

Marriages

ARNOLD PEEL MULKEY, Millen, Ga., to Miss Victoria Davis of Morehead City, N. C., in Kingston, N. C., August 12.

FREDERICK MCCULLOCH MORRISON, Lynchburg, Va., to Miss Gertrude Davis Hancock of Beaufort, N. C., recently.

CHARLES GORDON MERRICK, Fort Myers, Fla., to Mrs. Elizabeth Woolslair Page in Jacksonville, September 8.

RUDOLPH DAVID MARTIN, Nanticoke, Pa., to Miss Helen Irene Gombar of Throop, August 7.

THOMAS LAWMAN LUCAS to Miss Jane Hill Agnew, both of Charleston, S. C., August 31.

WILLIAM C. MCCONNELL to Miss Gladys Behlmer, both of Sunman, Ind., September 24.

JOHN I. LIMBURG JR., to Miss Frieda Schere, both of Cedar Bluffs, Iowa, recently.

PHILIP L. KURTZ to Miss Jane Elizabeth Walker, both of Indianapolis, July 15.

Deaths

Henry J. Gahagan ⊕ Chicago; Rush Medical College, Chicago, 1893; practiced in Elgin, Ill., from 1897 to 1914, where he served as commissioner of health from 1897 to 1901, and city physician from 1901 to 1909; member of the American Psychiatric Association, member of its National War Work committee, 1917-1918, and chairman of its occupational therapy committee in 1918 and 1921; member of the medical house staff, attending physician, Elgin State Hospital, from 1893 to 1897, and superintendent from 1914 to 1917; medical director of the Mercyville Sanitarium, Aurora, since 1917; attending physician, consultant on the staff and member of the insanity committee of the Cook County Psychopathic Hospital; in 1916 was appointed by the board of administration of Illinois to visit the state institutions in New York, Pennsylvania, Maryland, Massachusetts and Ohio and report as to the industrial pursuits of patients; aged 68; was killed, November 10, when he was struck by an automobile as he alighted from a bus.

John Fairbairn Binnie, San Diego, Calif.; University of Aberdeen Faculty of Medicine, Scotland, 1886; began practice in Kansas City, Mo., in 1889; member of the Missouri State Medical Association; secretary of the Section on Surgery and Anatomy of the American Medical Association, 1908-1909; at one time professor of surgery at the University of Kansas School of Medicine, Kansas City, Kan.; formerly on the staff of the Kansas City (Mo.) General Hospital; organized Base Hospital 28 as a Red Cross unit before the war and directed the unit in France until he was assigned as surgical consultant to the third army corps; member of the American Surgical Association and the Society of Clinical Surgery; fellow of the American College of Surgeons; author of a widely known manual on "Operative Surgery"; aged 73; died, November 28.

Charles Griffin Plummer, Salt Lake City; Chicago Medical College, 1888; practiced at Salt Lake City since 1891; member of the Utah State Medical Association; for three years colonel in the first infantry of the Utah National Guard; member of the Utah State Commission for Feeble-Minded for four years; on the staff of the Latter-Day Saints Hospital; formerly regent to the University of Utah; awarded testimonial by citizens for service to community and work with youth; in 1935 was awarded twenty-five year veteran silver badge by the National Council, Boy Scouts of America; aged 77; died, November 19.

Harper M. Workman ⊕ Tracy, Minn.; Chicago Medical College, 1878; member of the House of Delegates of the American Medical Association, 1905-1906; secretary of the Lyon-Lincoln Counties Medical Society; councilor of the third district and past president of the Minnesota State Medical Association; fellow of the American College of Surgeons; first mayor of Tracy; for many years president of the school board; aged 81; died, October 8, of myocarditis and nephritis.

Eugene Garfield McKeown ⊕ Pipestone, Minn.; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1909; fellow of the American College of Surgeons; formerly secretary of the Southwestern Minnesota Medical Society; county health officer; served during the World War; medical director of the Pipestone Indian Hospital; on the staff of the Ashton Memorial Hospital; aged 55; was killed, October 20, in an automobile accident.

Chester Sylvester Leach ⊕ Brattleboro, Vt.; University of Vermont College of Medicine, Burlington, 1899; past president and secretary of the Windham County Medical Society; vice president of the New England Physical Therapy Society; at one time district health officer; roentgenologist to the Brattleboro Memorial Hospital; aged 60; died, October 23, in the Baker Memorial Hospital, Boston, of coronary embolism.

Bernard Anthony O'Hora, Detroit; Washington University School of Medicine, St. Louis, 1917; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; served during the World War; at various times on the staffs of the Woman's Hospital, Children Hospital, Henry Ford Hospital and Harper Hospital; aged 47; died, October 29, of rheumatic heart disease.

Charles Edward Woodbury, Acworth, N. H.; University of the City of New York Medical Department, 1873; member of the Rhode Island Medical Society; at one time inspector of institutions for lunacy and charity in Massachusetts; formerly superintendent of the Rhode Island Hospital, Providence, and the Foxboro (Mass.) State Hospital; aged 90; died, October 31, at the home of his daughter in Roslindale, Mass.

John A. Klump, Williamsport, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1881; past president of the Lycoming County Medical Society; consulting surgeon to the Williamsport Hospital; fellow of the American College of Surgeons; aged 80; died, October 21, in the Danville (Pa.) State Hospital, of cerebral arteriosclerosis and bronchopneumonia.

Duncan Campbell, Woodbury, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1895; member of the Medical Society of New Jersey; for many years lecturer on medical terminology at his alma mater; formerly on the staff of the Underwood Hospital; aged 69; died, October 30, in the Broad Street Hospital, Philadelphia, of cerebral hemorrhage.

James Garfield Paschen, Wauwatosa, Wis.; Milwaukee Medical College, 1908; member of the State Medical Society of Wisconsin; associate member in medicine on the staff of Mount Sinai Hospital, Milwaukee; aged 51; died, October 28, in the Columbia Hospital, Milwaukee, of cerebral hemorrhage and splenomyelogenous leukemia.

David Judson Barton, Anderson, S. C.; University of Georgia Medical Department, Augusta, 1906; member of the South Carolina Medical Association; president and formerly secretary of the Anderson County Medical Society; at one time on the staff of the Anderson County Hospital; aged 54; died, October 23.

John Milton Holt, Los Angeles; Long Island College Hospital, Brooklyn, 1895; served during the World War as director of sanitation for the Houston extracantonment zone; formerly city health officer; for many years attached to the U. S. Public Health Service; aged 63; died, October 15, of coronary occlusion.

David Clarence Confer, Duncansville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1881; member of the Medical Society of the State of Pennsylvania; formerly postmaster, member of the school board and secretary of the board of health; aged 79; died, October 23.

Frank Clifford Walker, Windsor, Vt.; Boston University School of Medicine, 1884; for many years health officer of Windsor; at one time city physician in Taunton, Mass.; formerly on the staff of the Morton Hospital, Taunton, Mass.; aged 78; died, October 19, of coronary occlusion.

Frederick Harvey ⊕ Chicago; Chicago College of Medicine and Surgery, 1915; fellow of the American College of Surgeons; served during the World War; member of the attending staff of the Grant Hospital; aged 46; was killed, December 9, in an automobile accident.

William James Renwick McFarland, Syracuse, N. Y.; Baltimore Medical College, 1897; member of the Medical Society of the State of New York; on the staff of the People's Hospital; aged 63; died, October 23, of carcinoma of the pancreas and obstructive jaundice.

Joseph Benjamin Moxley, Brantley, Ala.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1899; member of the Medical Association of the State of Alabama; formerly member of the state legislature; mayor of Brantley; aged 58; died suddenly, October 30.

John King Stewart, Tacoma, Wash.; Hahnemann Medical College and Hospital, Chicago, 1910; member of the Washington State Medical Association; served during the World War; aged 68; died, October 21, in the Tacoma General Hospital, of acute coronary thrombosis.

Edward James Delaney, Concord, N. H.; Baltimore Medical College, 1903; member of the New Hampshire Medical Society; for many years physician to the state prison; on the staff of the Mary Pillsbury Hospital; aged 58; died, October 21, of cirrhosis of the liver.

Richard Joseph Shannahan, Worcester, Mass.; Columbia University College of Physicians and Surgeons, New York, 1903; member of the Massachusetts Medical Society; for many years a police surgeon; aged 57; died, October 31, of arteriosclerotic heart disease.

Augustus Woodbury Calder, Providence, R. I.; Harvard University Medical School, Boston, 1895; member of the Rhode Island Medical Society; veteran of the Spanish-American and World wars; aged 67; died, October 25, of coronary occlusion and arteriosclerosis.

Leo Schram ⊕ Dayton, Ohio; Hahnemann Medical College and Hospital, Chicago, 1892; past president of the Montgomery County Medical Society; city physician; for many years on the staff of the Miami Valley Hospital; aged 68; died, October 5, in Russels Point.

Antoine A. Laurent ⊕ Minneapolis; Minneapolis College of Physicians and Surgeons, 1911; member of the staffs of St. Mary's, St. Barnabas, Northwestern and Deaconess hospitals; aged 54; died, October 21, of coronary thrombosis and arteriosclerosis.

James Logan McMillan ⊕ Decaturville, Tenn.; College of Physicians and Surgeons, Memphis, 1907; past president and secretary of the Decatur County Medical Society; aged 51; died, October 31, in the Protestant Hospital, Nashville, of neurofibroma.

Joseph Foster Grant, San Diego, Calif.; University of Louisville (Ky.) Medical Department, 1890; fellow of the American College of Surgeons; served during the World War; on the staff of the San Diego County Hospital; aged 67; died, October 27.

David Lyle, Rock Hill, S. C.; Medical College of the State of South Carolina, Charleston, 1909; formerly member of the state legislature, and mayor of Rock Hill; on the staff of St. Philip's Mercy Hospital; aged 57; died, October 25, of angina pectoris.

Herbert Elton Doty, Concordia, Kan.; Ensworth Medical College, St. Joseph, Mo., 1906; member of the Kansas Medical Society; county coroner; aged 67; on the staff of St. Joseph's Hospital, where he died, October 19, of chronic myocarditis.

Albert Eugene Fuchs ⊕ Bunker Hill, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; formerly a practitioner in Chicago; aged 61; died, October 27, of diabetes mellitus.

August Liliencrantz, Oakland, Calif.; Rush Medical College, Chicago, 1870; member of the California Medical Association; aged 89; died, October 9, in Peralta Hospital, of a skull fracture received when struck by an automobile.

Fredrick Cushman Kinney, Hardwick, Vt.; University of Vermont College of Medicine, Burlington, 1882; member of the Vermont State Medical Society; aged 78; died, October 21, in the Hardwick Hospital, of cerebral hemorrhage.

Mary Frances Deraismes Thornton, Albany, N. Y.; Cornell University Medical College, New York, 1902; aged 62; died suddenly in October in New York of fracture of the neck of the femur and coronary sclerosis.

Olav S. Behrentz, Three Rivers, Mich.; Rush Medical College, Chicago, 1903; for many years a medical missionary in China; aged 63; died, December 8, in the Presbyterian Hospital, Chicago, of coronary sclerosis.

Arthur Elias Henby, Seattle; Chicago Homeopathic Medical College, 1897; member of the Washington State Medical Association; served during the World War; aged 62; died, October 8, of coronary disease.

Howard Leonard Reed, Henrietta, Texas; University of Oklahoma School of Medicine, Oklahoma City, 1916; served during the World War; aged 52; died, October 23, in a hospital at Wichita, of pneumonia.

Victor Mackay Daly, Pontiac, Ill.; University of Edinburgh Faculty of Medicine, Scotland, 1892; served during the World War; on the staff of St. James Hospital; aged 69; died, October 22, of heart disease.

Nathaniel Hooks Lozier, Sandersville, Ga.; Atlanta Medical College, 1914; member of the Medical Association of Georgia; aged 46; died, October 21, at a hospital in Atlanta, of a streptococcic infection.

Jonathan Jay Pitcher, Mount Pleasant, Iowa; Hahnemann Medical College and Hospital, Chicago, 1906; member of the Iowa State Medical Society; aged 54; died suddenly, October 22, of a cerebral hemorrhage.

Norman Bates Dresser, Berlin, N. H.; Medical School of Maine, Portland, 1919; formerly county coroner and city health officer; aged 41; was found dead in bed, October 20, of acute dilatation of the heart.

George A. Downs, Spokane, Wash.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; served during the World War; aged 59; died, October 18, of disseminated sclerosis.

William Owen Wisner, Spokane, Wash.; Medical Department of Omaha University, 1892; formerly county health officer; aged 71; died, October 17, in the Sacred Heart Hospital, of lobar pneumonia.

Adolph W. Hanson, Portland, Ore. (licensed in Minnesota by years of practice); (licensed in Iowa in 1898); aged 76; died, October 8, of cardiovascular renal disease and cerebral hemorrhage.

Edwin Eli Wilcox, Salt Lake City; University of the City of New York Medical Department, 1894; on the staff of the Dr. W. H. Groves Latter-Day Saints Hospital; aged 71; died, October 7.

Charles Lindley Johnston, Plattekill, N. Y.; University of Michigan Homeopathic Medical School, Ann Arbor, 1884; aged 78; died, October 24, of paralysis agitans and cardiac dilatation.

Albert Nicholas Jacob ⊕ Sparta, N. J.; Jefferson Medical College of Philadelphia, 1888; past president of the Sussex County Medical Society; aged 72; died, October 27, of coronary embolism.

James D. McKie, Vanndale, Ark.; University of Louisville (Ky.) School of Medicine, 1876; member of the Arkansas Medical Society; aged 84; was killed, October 14, when struck by a train.

George Albert McLane, Harvard, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; aged 60; died, October 2, of chronic nephritis.

Charles Augustus Lerch, Akron, Ohio; Cincinnati College of Medicine and Surgery, 1877; aged 84; died, October 21, in the City Hospital, of hypostatic pneumonia following a Colles fracture.

Leslie Allen Wilson ⊕ Cameron, Mo.; Northwestern University Medical School, Chicago, 1921; secretary of the Clinton County Medical Society; aged 45; died in October of heart disease.

George W. Smith, Washington, D. C.; Howard University College of Medicine, Washington, 1885; aged 81; died, October 8, in the Garfield Hospital, of carcinoma of the bladder.

Samuel W. Dunlavy, Coffeyville, Kan.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1902; aged 63; died, October 31, of acute dilatation of the heart.

William P. Miles Jr., New Orleans; University of Maryland School of Medicine, Baltimore, 1890; aged 69; died, October 4, of cerebral thrombosis and arteriosclerosis.

Frank Segel Smith, St. Peter, Ill.; Kentucky School of Medicine, Louisville, 1892; county coroner; aged 70; died, October 26, at Vandalia, of heart disease.

Henry J. Leigh, Tower City, N. D.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1891; aged 70; died, October 22, of carcinoma of the stomach.

Paul Lannom Dickson, Los Angeles; Barnes Medical College, St. Louis, 1900; aged 60; died, October 22, in the Good Samaritan Hospital, of heart disease.

Gipson W. Stagner, Richmond, Ky.; Louisville Medical College, 1890; aged 75; died, October 31, in the Good Samaritan Hospital, Lexington, of uremia.

Thomas A. Lynch, Brooklyn; Long Island College Hospital, Brooklyn, 1908; served during the World War; aged 51; died, October 28, of heart disease.

George Logan Hall, Baltimore; Howard University School of Medicine, Washington, D. C., 1914; aged 51; died, October 31, of aortic insufficiency.

Albert E. Byron, Oakland, Calif.; California Eclectic Medical College, Los Angeles, 1895; aged 64; died, October 28, of a self-inflicted bullet wound.

Henry R. Riemer, St. Joseph, Mo.; Ensworth Medical College, St. Joseph, 1897; also a minister; aged 90; died, October 29, of arteriosclerosis.

Gustavus Adolphus Spivey, Dallas, Texas; University of Louisville (Ky.) Medical Department, 1876; aged 85; died, October 24, of senility.

Abner Jackson Mynatt, Lamar, Mo.; University Medical College of Kansas City, 1898; aged 67; died, October 14, of heart disease.

Edward Wenger, St. Louis; Beaumont Hospital Medical College, St. Louis, 1890; aged 68; died suddenly, October 17, of heart disease.

T. I. Mohler, Palestine, Ark. (licensed in Arkansas in 1903); Civil War veteran; aged 92; died, October 19, of arteriosclerosis.

John E. Westaver, St. Louis; St. Louis College of Physicians and Surgeons, 1898; aged 84; died, October 10, of general debility.

Fred Ernest Zumstein, Detroit; Miami Medical College, Cincinnati, 1900; aged 70; died, October 30, of cerebral hemorrhage.

Correspondence

"AUTOGENOUS SERUM TREATMENT OF NARCOTIC ADDICTION"

To the Editor:—In THE JOURNAL, October 17, page 1337, appeared a lengthy abstract on Autogenous Serum Treatment of Narcotic Addiction (Black, D. M.: *Canad. M. A. J.* **35**:177 [Aug.] 1936). I believe that the purpose of Current Medical Literature is to advise readers of advances or new treatments published elsewhere. The following will make clear my object in writing:

According to *La tribune médicale* (December 1929, p. 564) Modinos first called attention to the therapeutic value of serum from blisters some twenty years before this article (1929). Lassablière called attention to this treatment in *Médecine* (December 1928). Modinos reports eight cases of narcotic addiction treated by this method; three of these cases are given in considerable detail.

Based on these reports, I tried this treatment in 1933 in a case of diacetylmorphine addiction. While the cantharides plaster produced an acceptable blister, the restlessness of the patient during the night made him burst the blister. On repetition of the experiment the same unsatisfactory results were obtained. I then considered using his own whole blood. Withdrawal of the 10 cc. was successful, but the blood immediately coagulated in the syringe. Since a foreign protein appeared to be the basis of treatment, I then used 10 cc. of boiled milk intramuscularly with some success. This dose was repeated three times. This case, however, proved to be one of those unmanageable ones, and the patient continued his addiction.

Shortly after I used boiled milk again in a similar case. Four injections, together with phenobarbital by mouth, gave satisfactory results, and the patient had no more desire for narcotics.

In the third case of diacetylmorphine addiction, the patient, treated like the other two, abstained from narcotics for thirty days but then relapsed. Since the drug appears to be well eliminated from the system after such an interval, other reasons for his return to the drug have to be considered.

Lest some one thinks that my treatment is new, I wish to mention Amsler, C.: Zur Frage der Entwöhnung von narkotischen Giften (*Klin. Wchnschr.* **13**:773 [May 26] 1914). He states that Biberfeld used the protein of goat milk parenterally with success. This article came to my attention after the treatment of the three cases mentioned.

HANS SCHROEDER, M.D., San Francisco.

DETERMINATION OF GALACTOSE IN URINE

To the Editor:—My attention has been called independently by Dr. Walter R. Johnson of Asheville, N. C., and Dr. Hans Wassing of Paterson, N. J., to an error in my article on "Painless Jaundice," which appeared in THE JOURNAL, May 11, 1935, p. 1681. In that article I stated that "the determination of galactose in the urine is done exactly like the quantitative determination for dextrose; the only modification is that, because of the greater reducing power of galactose, it is necessary to multiply the result by 0.7."

Dr. Wassing calls my attention to wide discrepancies in practice in different laboratories and in different textbooks. Thus, he says that Gradwohl in his textbook states that 25 cc. of Benedict's reagent is reduced by 54 mg. of galactose. Therefore, one would use a correction of 1.1. Wassing himself found approximately the same, 55 or 56 mg. of galactose reducing 25 cc. of the reagent.

Mattice in his "Chemical Procedures for Clinical Laboratories," Philadelphia, Lea & Febiger, 1936, page 66, says: "5 ml. of Benedict's quantitative reagent are reduced by 12.5 mg. of galactose." This would correspond to 25 cc. of the reagent being reduced by 62.5 mg. of galactose and would give a correction of 1.25.

I asked Dr. Sobotka, chemist at Mount Sinai Hospital, to investigate this question and his assistant, Miss Miriam Reiner, writes me as follows:

> The galactose used in these experiments was *d*-galactose c. p. Pfanstiehl with a specific rotation plus 80.5°. This sugar had previously been dried over phosphorus pentoxide in a desiccator. The galactose was carefully weighed and the solution was checked in the polariscope; 2 per cent solution in a 2 cm. tube had a specific rotation of plus 80.5°.
>
> The Benedict reagent was first checked with a glucose solution; 25 cc. was reduced by 50 mg. of glucose. When the galactose solution was used, 65 mg. were necessary to reduce the same amount of Benedict's. Since galactose has a lower reducing value than glucose, the factor is glucose: galactose as 50 mg.: 65 mg., or 1: 1.30.
>
> Since the main contaminant of commercial galactose is glucose, the reducing factor of such a sugar would approach the glucose factor, depending upon the amount of glucose present in the sample. The specific rotation of galactose is plus 80.5° and that of glucose is plus 52.5° so that the presence of glucose would lower the specific rotation of the sugar sample.
>
> After taking all these factors into consideration, and comparing my standard galactose with a similar glucose solution, I think we can safely say that the galactose factor for Benedict's quantitative sugar reagent is 1.30.

REUBEN OTTENBERG, M.D., New York.

WATER FILTRATION VS. CHLORINATION

To the Editor:—My attention has been called to the editorial "Water Filtration vs. Chlorination," which appeared in THE JOURNAL, October 31. The citation of Altona, Germany, as an example of a case in which filtration failed to give adequate public health protection is hardly justified by the reported facts of the classic Hamburg-Altona cholera epidemic of 1892. The Altona experience should properly be cited as a classic example of the public health benefits of filtration and not its limitations. This epidemic preceded both the advent of chlorination for public health purposes and important developments in rapid sand filtration commonly used today.

The outstanding record of water filtration in reducing the typhoid and general death rate in cities where water from polluted sources was formerly used is one of the greatest achievements in public health in America, and much of this was accomplished before chlorination was practiced. It is hardly possible to put chlorination and filtration on the same comparative plane. In modern water works practice the two processes logically go together and in no sense are competitive in meeting modern standards of public health for water supplies. Chlorination is an effective sterilizing agent and its cost in treating public water supplies is almost insignificant in proportion to the benefits derived. Filtration in its broadest sense is a complete process of purifying water including safety, palatability and physical appearance, and the use of chlorine is usually implied when the water is used for domestic purposes.

From a public health standpoint, all public water supplies should be chlorinated. Chlorination, since its first use in water sterilization in 1908, has developed to be one of the greatest factors in safeguarding the public health of cities and communities. But chlorination has its limitations and they must be recognized. Chlorination within practical limits does not destroy certain resistant microscopic organisms found in water, especially Bacillus welchii and the cysts of Endamoeba histolytica, which are of public health significance. Chlorine or chlorine compounds may result in objectionable tastes in water either through the use of large quantities or as a result of combination with other substances, especially in water pol-

luted by sewage and industrial wastes. It does not remove objectionable tastes and odors such as oil refinery wastes. Chlorine is rapidly absorbed by dissolved and suspended matter in the water, especially by organic compounds.

Not all water supplies, especially ground water, may need filtration, but most surface water supplies regardless of their source can be markedly improved in taste and physical appearance and safety at moderate expense through filtration. Any source of public water supply that is exposed to pollution or objectionable turbidities should be filtered as well as chlorinated. Chicago is a good example. Lake Michigan, the source of supply, is normally clear, but the water at the city's intakes is at times polluted by sewage and industrial wastes and is frequently turbid to an objectionable degree. Chlorination is a public health necessity. Effective chlorination is complicated and difficult in spite of rigid control measures, because of the wide variation in the chlorine demand of the lake water. If this demand were to exceed the chlorine dosage applied to the water, the sterilizing action would be very much limited. A serious health risk exists every time sudden and excessive pollution of the lake waters in the vicinity of the intakes occurs. These periods can be foreseen to some extent but not always, and there is a decided element of risk connected with dependence on chlorination alone. Filtration would correct this condition.

In a filter plant, the time of passage through the settling basins and filters gives the chemist an opportunity not only to sterilize and clarify the water but also to treat it to remove all tastes. This time interval permits adjustment of treatment to correct for sudden changes in the character of the raw water. With intelligent operation a uniformly clear palatable and safe water can be supplied at all times. Filtration permits the maintenance of a clean distribution system and thus clean water through to the tap of the ultimate consumer. Such a condition is not true of chlorinated unfiltered surface waters and frequently of clear ground waters. Raw natural waters of this type frequently cause growths and deposits in mains. Surface waters that may look clear in the glass usually contain large numbers of micro-organisms in suspension. These will settle out in zones of low velocity in a distribution system, decay and cause a fishy, grassy taste in the water and a discoloration that is very objectionable to the consumer.

It is true that many water outbreaks in recent years have been caused by pollution of water en route to the consumer through cross connections with the public distribution system. This is a regrettable condition but one that has nothing to do with the merits of chlorination as against filtration without chlorination, which is doubtful practice. By using the ammonia-chlorine processes for treating the filtered water, residual chlorine can be carried throughout a distribution system without causing objectionable tastes in the water. But this process requires several hours for effective bactericidal action. With a filtration plant this retention period is provided. The cost of complete purification of a public water supply is so low in comparison with the benefits to be derived that the economics of chlorination versus filtration should hardly be considered, especially where the public health is threatened.

ARTHUR E. GORMAN, B.S., Chicago.

To the Editor: I have noted with interest the editorial which appeared in the October 31 issue of THE JOURNAL entitled "Water Filtration vs. Chlorination." Owing, however, to the occurrence of a factual error in the reference to the 1892 epidemic of cholera in Altona, Germany, and the consequent reflection on the effectiveness of filters in the purification of water, it is thought that you might wish to present the following comment to your readers.

The cholera epidemic occurring in Germany in 1892 was the first practical demonstration of the effectiveness of filtration in the prevention of water-borne disease. The city of Hamburg, supplied with unfiltered water from the Elbe River, experienced a severe epidemic of cholera, whereas no such epidemic occurred in the neighboring community of Altona, served with the same water after filtration through slow sand filters. Furthermore, the editorial mentioned may be misleading in that it implies that all public water supplies may be effectively chlorinated and that filtration is needed merely to clarify the water and produce a water which is attractive to the consumers.

In general, both chlorination and filtration of water have inherent weaknesses which must be recognized. As a result, both methods of treatment are normally required when polluted surface waters are being treated. This fact may be overlooked, however, and undue confidence placed in the effectiveness of chlorination alone. This justifies a brief statement as to the limitations of chlorination alone, which is inherently subject to interruptions because the failure of chlorine treatment results at once in the delivery of untreated raw water, whereas ineffective filtration is at least partially effective. The effectiveness of chlorination is influenced to a marked extent by the fact that the chlorine dose must be varied under adequate control to compensate for changes in the chlorine demand of the water, which fluctuates with the organic content, temperature and p_H value of the water. Furthermore, suspended solids in the raw water, especially those which may protect bacteria associated with pollution, interfere with the disinfecting action and prevent chlorine reaching the embedded bacteria, unless the dose is higher than permissible from the standpoint of the production of a tasteless water. My point is that chlorination must be used in conjunction with filtration when the average surface water is being treated. It is for this specific reason that Milwaukee is now constructing a filtration plant and that a similar plant is being advocated for Chicago.

Fortunately, an approximate quantitative estimate may be made as to the effectiveness of chlorination alone, and of chlorination when combined with rapid sand filtration, as a result of studies by the United States Public Health Service at Cincinnati, Ohio. For instance, these studies indicate quite clearly that the average surface water cannot be effectively chlorinated in the absence of filtration, unless the average number of organisms of the coli-aerogenes group is less than from 80 to about 100 per hundred cubic centimeters of water, provided the number of such organisms in the raw water is less than 450 per hundred cubic centimeters 95 per cent of the time. On the other hand, filtration combined with chlorination permits the effective treatment of a much more heavily polluted water, because with this more complete treatment the average number of organisms of the coli-aerogenes group of the raw water may be from 3,500 to 5,000 per hundred cubic centimeters of water, provided the maximum number of such organisms is less than 20,000 per hundred cubic centimeters 95 per cent of the time.

If the foregoing standards as to the degree of pollution of the raw water are complied with, the treated water will meet the Treasury Department standards as to the quality of water permissible for use on interstate carriers.

I have discussed this matter at considerable length because it is very desirable that the confidence of the public in the effectiveness of filtration plants be maintained and that undue confidence may not be placed in the effectiveness of the chlorination of the average surface water.

PAUL B. BROOKS, M.D., Albany, N. Y.
Deputy Commissioner of Health,
State of New York.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TRAUMA AND ABORTION

To the Editor:—A woman, aged 24, whom I had never seen or examined before, had an incomplete abortion of about three and one-half to four months. She gave the history of having fallen from a boat to a stone wharf, a distance of about 3 feet. She states that she fell on her abdomen. I said at the time, and I still feel, that the fall per se did not produce or induce the abortion. But I do not feel that all these cases are caused by distinct pathologic entities, endocervicitis, and so on. Later curettage was done and the secundines were examined microscopically. This case is coming up for trial as the woman is suing the ferry boat company for negligence and stating that the fall is the cause of the abortion. I imagine her lawyers will ask me if a fall could cause an abortion, or, since I never examined the woman before, how could I say anything else than that the fall caused abortion? How long after a fall could it be precluded that the fall was the cause of the abortion? What would you advise as to the position I should take on this matter? Please give reasons. I mean medically and not legally or from a legal standpoint. Would the length of time the patient was pregnant have any bearing on this type of abortion? Have you any figures on this? Please omit name.

M.D., Ohio.

ANSWER.—When suits of this type arise, the following points must be determined if possible: (1) the existence of pregnancy prior to the accident, (2) the presence or absence of signs or symptoms of abortion prior to the accident, (3) the presence or absence of factors predisposing to abortion aside from the alleged cause, and (4) the actual occurrence of abortion. Since the correspondent had not examined the patient before the accident he will be unable to testify that she was three or four months pregnant before the accident. He will be unable to vouch for the presence or absence of signs or symptoms of abortion prior to the accident. In considering possible factors in abortion he should try to determine the following: (1) abnormality of the fetus, such as knotted cord, deformity, or other anomaly that could not be the result of trauma to the mother; (2) abnormality of the placenta, such as syphilis or tuberculosis; (3) constitutional factors in the mother predisposing to abortion, such as dietary or vitamin deficiency, or history of previous abortion; (4) existence of focal infections, which are sometimes held responsible for abortion; (5) existence of pelvic abnormalities such as myoma, cysts, cervicitis, severe lacerations, pelvic inflammatory disease and (?) retroversion; (6) systemic diseases, such as syphilis, tuberculosis or toxemia of pregnancy; (7) exposure to toxic agents, such as lead, irradiation, too much alcohol or nicotine; (8) previous operative procedures, such as trachelorrhaphy; (9) intercourse immediately prior to abortion, and (10) vigorous douching with cold or hot water. The possibility of induced abortion prior or subsequent to the accident must be remembered. Since retained secundines were removed and examined microscopically, the physician can testify factually regarding the existence of pregnancy. That is almost the only unqualified statement that he can make. His opinion will be based largely on the presence or absence of the predisposing factors enumerated. For authorities he may consult Taussig (Abortion, Spontaneous and Induced, St. Louis, C. V. Mosby Company, 1936, p. 114): "That [external injury or strain] is often an important contributing factor in the initiation of uterine contractions cannot be gainsaid. But in most instances a careful analysis will show other more fundamental causes. One may well be skeptical of the effect of even rather violent external trauma in the production of abortion since we have so many instances in which internal manipulations such as curettement have failed to bring on an abortion." Taussig (p. 114) quotes Seitz that the greatest tendency for traumatic interruption of pregnancy is in the first sixteen weeks, even though at this time the uterus lies more protected in the pelvic cavity than later. Taussig says "Sexual intercourse is probably one of the most positive direct traumatic agents productive of abortion" (p. 114). He considers "psychic trauma" an undoubted factor. D. M. Lindsay (Trauma and Compensation in Obstetric and Gynaecological Cases, Edinburgh and London, William Hodge & Co., Limited, 1928, pp. 41-42) says "Possibly the proper view to accept [regarding fright, fall or injury] is that accident as a cause of such complication [abortion] is rare in the absence of some already predisposing factor, but that it can cause miscarriage without other predisposing factors I am satisfied." J. R. Miller gives a good list of references (Trauma and Compensation in Gynecology and Obstetrics, *Am. J. Obst. & Gynec.* **26**:839 [Dec.] 1933). Presumably a trauma severe enough to cause abortion would promptly produce abortion. No time limit can be stated because of the possibility of missed abortion with a long latent period. The physician in the present case will do well to confine himself to facts and state his own opinion cautiously.

PERSISTENT YAWNING

To the Editor:—I have a case of hysteria manifested by continuous yawning, which began about five months ago following recovery from a successful operation for removal of the gallbladder. The yawning becomes so severe at times that the jaws become painfully sore. Sedatives give only temporary relief. Endocrine therapy has not seemed to help any. I am unable to find any foci of infection. I would appreciate any suggestions you may offer.

M.D., Louisiana.

ANSWER.—In normal persons and other animals, yawning is essentially an involuntary deep inspiration accompanied by wide opening of the mouth and frequently stretching of the body musculature. The conditions leading to this act are usually marked mental and physical weariness or fatigue, such as may be brought on by prolonged mental or physical exertion, low blood pressure or some degree of tissue asphyxia. The performance of this act in one individual has a peculiar suggestive potency in others, leading to the same act in them, if conditions are favorable. Persistent yawning in hysteria is usually only one (and not a frequent) manifestation of hysteria. There is no known reason why hysterical yawning should be connected with convalescence from a gallbladder operation, unless the operation resulted in prolonged low blood pressure or interference with the respiration leading to tissue asphyxia, in which case, in a susceptible person, the yawning may have been established as a habit; but this would scarcely be called true hysteria. Endocrine therapy in this condition would be purely empirical and sedatives, of course, of only temporary value. If the patient is more or less depressed, thyroid therapy might help a little. If there is interference in circulation or respiration, stimulants should act more favorably than sedatives. If it is a habit developed during a long period of convalescence, stimulants and cheerful and interesting surroundings might help to overcome the habit. If it is true hysteria and the person manifests other indications, such as chronic fatigue and depression, one should try vasomotor and central nervous system stimulants and a cheerful and stimulating environment, combined with the usual psychomotor reeducation therapy, sometimes effective in hysteria.

INVERTED VISION

To the Editor:—A boy who will be 9 years old next January and is now in the third grade is a very good student—about B or B plus. Within the last three weeks he has taken to turning his book upside down to read. He also inverts his number book. He reads from the blackboard and only seldom tells the teacher that she is writing upside down. He reads numbers from the blackboard and usually gets the work done right side up on paper. Only once has he written his name upside down. He plays an instrument and tells his mother that he doesn't see how she can play music upside down. He was reading a book. I asked him what the story was about and I took the book and looked at it and handed the book back to him right side up. He said he couldn't read the book upside down and proceeded to invert it and read. I do not think a youngster of that age would think of this as a means of gaining attention and be so consistent in it.

M.D., Louisiana.

ANSWER.—Cases of reversals and inversions in reading are not uncommonly found in a large school system; in fact, their occurrence is sufficiently frequent so that considerable work has been done by educational psychologists with reference to this problem. There are several theories as to its causation, the most prominent of which has to do with cerebral dominance. Some observers seem to think that inversions or reversals occur in left handed individuals who are compelled to use the right hand or vice versa. Others who distinguish the problem of "eyedness" from "handedness" seem to think that, although the individual may be using the proper hand, contralateral eye dominance may be present, which adds to the confusion. After an emotional upset or an acute ailment a suppressed eye or hand dominance may cause a sudden change in the capacity to read or to see right side up or from right to left. Some have shown that improper teaching methods are extremely important. Again, lack of fusion in which the retinal image of one eye is confused with the other because of muscle impairment or some other ocular defect may be significant. Bad home or school conditions, both patent and latent, may lie behind the emotional upset, which in turn may not be readily apparent to the inexperienced examiner.

A diagnosis of this condition and an analysis of its cause would have to be made on the basis of careful ophthalmic and physical examination, an analysis of the history by a psychiatrist who is skilled in dealing with reading disabilities and who is familiar with child behavior disturbances, in addition to a psychologic study by a psychologist who is a specialist in "corrective reading." The treatment usually is a matter of reeducation after any obvious cause has been removed, and this reeducation brings into account the use of kinesthesis both of the tongue and of the general body musculature. Home trial and error methods of correction are not only contraindicated but may actually cause emotional and other disturbances which may be worse than the immediate disorder, but it must not be forgotten that a condition of this sort may correct itself, although this is not usually the case. This means that it is better to neglect the problem than to "tinker." It must be remembered that this type of condition can occur in children of 9 or even younger as an attention-gaining mechanism and that it often requires a careful analysis of the emotional milieu of the child to see what the situation is that lies behind it. It would be advisable for the physician, if he has time, to check over some of the references in Marion Monroe's book "Children Who Cannot Read" dealing with this problem. Perhaps there is a large school system not too distant where there is a reading specialist who can give immediate advice.

SENSITIVITY TO BLOOD AND SERUM

To the Editor:—As an intern in 1931 I observed in the dispensary that occasionally I would develop a more or less severe localized skin reaction, with redness, itching and burning, to the blood of certain patients. The reaction did not occur always even though in some cases the blood was allowed to remain for some time; in other cases, itching would call my attention almost at once to blood stains, usually on the inner surface of the arm. I was interested in the phenomenon and thought that I might at some time investigate it thoroughly. My attention has again been called to this idea of allergic reaction by two rather recent cases of atypical reaction following blood transfusions. One occurred in a tuberculous patient, almost immediately after transfusion, as an acute pulmonary edema; the other happened not long afterward to another patient with traumatic hemothorax as a fairly typical asthma, several hours after blood transfusion, and responded to atropine sulfate (ephedrine was not given for fear of raising the blood pressure). Can you tell me whether anything has been done in the line of skin sensitivity to blood? It seems that there are other incompatibilities besides that disclosed by blood grouping and cross agglutination. I have talked with several pathologists and they said that the idea was entirely new to them.

MARGARET F. BENJAMIN, M.D., Muncie, Ind.

ANSWER.—Positive skin reactions to human blood serum with a positive complement fixation reaction was reported by György and Witebsky (*München. med. Wchnschr.* **50**:599, 1924) in one case. The two specimens of blood were of the same group. One blood transfusion caused no trouble. The second blood transfusion, twenty days later, was followed by a severe anaphylactic reaction, which however, was not fatal. The authors believe that the child was sensitive to some substance present in the serum itself or to some food present in the serum to which the child was sensitive. It is barely possible that the inquirer may be highly skin sensitive, without necessarily having clinical symptoms, to certain foods that may be present at various times in sufficient concentration in the serums with which she has come in contact to produce skin reactions. This assumption is highly speculative, as there is great dilution of such foods by the blood serum.

Regarding the second part of the inquiry, it is not stated whether the donors were merely typed or whether compatibility tests were done in addition. Occasional reactions may occur when universal donors (group O) have a very high titer of agglutinins or hemolysins in their serum, so that dilution by the recipient's blood is insufficient. A similar reaction may occur in universal recipients (group AB) when the donor's serum may be unusually high in agglutinins of hemolysins, so that dilution in the recipient's blood is insufficient.

In addition, one must consider the possibility of the presence in the donor's blood of "extra agglutinin 1." This was discovered in occasional bloods of groups O, A and B by Landsteiner and Levine. It is demonstrable when compatibility tests are done at temperatures of from 25 to 30 C. They may not be detected when tests are done at room temperature. Fortunately, reactions do not occur at a temperature above 30 C. The subject of anomalous agglutinins is however still under investigation, and occasional reactions occur which are not explainable by our present knowledge.

Reactions of an allergic nature may occur if the donor, previous to the transfusion, has ingested some foods to which the recipient is sensitive (Duke and Stoffer: *M. Clin. North America* **7**:1523, 1924). In addition, it may be possible to induce a state of passive sensitization by transfusing the blood of an allergic individual. The recipient may develop a reaction in the presence of the antigen. If, for instance, the blood of a cottonseed sensitive patient is used, the recipient may in a few hours develop symptoms from contact with a cotton filled mattress.

Reactions may also be due to citrated blood, to foreign matter present in the transfusion apparatus, either in the glass connections or in the rubber tubing, or to incipient coagulative changes in the blood as it passes through the apparatus (Satterlee, H. S., and Hooker, R. S.: Transfusion of Blood with Special Reference to the Use of Anticoagulants, THE JOURNAL, Feb. 26, 1916, p. 618).

DOSAGE OF BROWN MIXTURE FOR COLD

To the Editor:—Will you kindly send me a prescription of brown mixture for cold for an adult and state how often it must be taken? Also a prescription of brown mixture for children from 2 to 4 years old and how they must take it, as I am interested in a good formula of brown mixture. THOMAS GÄERSTE, M.D., Curaçao, Dutch West Indies.

ANSWER.—The formula for brown mixture or the compound mixture of opium and glycyrrhiza is to be found in the U. S. P. XI. Its composition is as follows:

Fluidextract of glycyrrhiza	120	cc.
Antimony and potassium tartrate	0.24	cc.
Camphorated tincture of opium	120	cc.
Spirit of ethyl nitrite	30	cc.
Glycerin	120	cc.
Distilled water....a sufficient quantity to make	1,000	cc.

While the dose of this mixture for an adult is a teaspoonful every two to four hours, one may give a child one or two drops of it for each year of age every two hours.

It should be understood, however, that it is not a cure for a cold in any sense of the word. It may, if taken with an abundance of fluid, tend to improve the secretion of the affected mucous membrane. It may lessen the violence of coughing; but, as colds are infections, the patient's system must acquire immunity. Toward immunization this medicine contributes nothing.

USE OF CAMPHOR IN OIL TO SUPPRESS LACTATION

To the Editor:—A white woman, aged 26, single, had a criminal abortion two years ago. The menstrual history is normal. Ever since the abortion the patient has observed a milky, watery discharge from the breasts, which is quite profuse at times. The breasts are not painful, or enlarged. The Wassermann reaction is negative. Physical and pelvic examinations are negative. Can you give me any suggestions as to the treatment for this condition? Please omit name. M.D., New York.

ANSWER.—Camphor in oil administered intramuscularly has a definite inhibiting effect on lactation. This effect appears to be due to a direct action of the drug on the secretory epithelium of the breasts. For the suppression of milk either immediately after the birth of a stillborn child or later when a child is weaned, L. G. McNeile (*West. J. Surg.* **43**:61 [Feb.] 1935) recommends that on the first day two 1½ grain (0.1 Gm.) doses of camphor in oil be injected intramuscularly, one in the morning and the other at night. On the second, third and fourth days one hypodermic of the same amount is given in the morning. If the breasts show any evidence of active function after the fourth day, an injection is given on the fifth and sixth days also. Since there is no harm in administering this form of therapy, it should be tried in the present case.

AGE OF LOSS OF POTENCY—MENOPAUSE

To the Editor:—1. What is the average age of beginning loss of libido or beginning impotence in males, without venereal history? 2. What is the average age at which women are considered past the childbearing age? M.D., New York.

ANSWER.—1. Normally the absence of libido and impotence should coincide, but this is by no means always the case. The trouble is when the libido continues but the power for connection is lost. In both conditions the onset is gradual and may be said to start at the age of 65. This age is the average age, but it is nothing unusual for men to be sexually active at 70, 80 or even later. Pathologically of course, even in the absence of any venereal disease, conditions may appear at early ages.

2. As a rule to which there are exceptions, women do not become pregnant after the menopause. Statistics from those who have investigated this point in hundreds of cases seem to indicate that in the United States the menopause comes on at the age of 50. Different countries and different races vary greatly in this regard.

ARTIFICIAL FEEDING OF INFANTS

To the Editor:—Is it the common practice of pediatricians in the United States to arrange the formula of bottled-fed infants so that they are given whole (cow's) milk at 5 months of age? I am assuming in this question that the infant must be put on the bottle from birth.

LEON PARIS, M.D., Bronx, New York.

ANSWER.—A normal, full term, bottle fed infant requires from 1½ to a maximum of 2 ounces of cow's milk per pound of body weight in twenty-four hours and a total fluid requirement of 3 ounces per pound of body weight. This means that the average 5 months old infant will receive from 24 to 30 ounces of cow's milk in twenty-four hours. The usual infant of this age will take five bottles of 7 ounces each, or a total of 35 ounces, which necessitates the adding of from 11 to 5 ounces of boiled water to the milk. Whole cow's milk is ordinarily not prescribed before the latter part of the first year, as gastric and intestinal digestion are usually not adequate for undiluted milk before this time.

URTICARIA

To the Editor:—A patient has severe urticaria and I have had no success whatever with the many known prescriptions. Suffice it to say that I have tried all therapy that is listed in the attempt to abort such a condition. I shall be grateful if you will suggest or furnish me any data that you have at your disposal. In addition, I shall be grateful for any intravenous or intramuscular medication that may be attempted in just such an affliction. I am most anxious to abort this condition. I may add that the patient has been previously diagnosed by another man as having petit mal and is a daily user of one tablet of phenobarbital. Does the latter bear any relation to the urticaria? If so, would it be advisable to substitute elixir of phenobarbital?

BENEDICT B. BACKLEY, M.D., Jacksonville, Ohio.

ANSWER.—Phenobarbital may be suspected as a possible cause of the urticaria. A patch test with phenobarbital might give some information as to its status in producing the eruption. If it is responsible for the dermatosis, the elixir of phenobarbital will produce the same effect. Intramuscular injections of epinephrine solution and intravenous injections of calcium gluconate solution or of the patient's own blood are worth trying.

TREATMENT OF EPIDIDYMITIS

To the Editor:—A man with acute gonorrhea has had prostatitis and unilateral epididymitis. His symptoms have improved until there is only slight tenderness in the epididymitis and in the prostate. A moderate discharge is still present. How soon will it be safe to attempt the passing of sounds? How often should the prostate and seminal vesicles be massaged? Please omit name.

M.D., Iowa.

ANSWER.—Unless the patient has a stricture there is little reason for passing sounds in this case. Routine massage of the prostate and vesicles, followed by an instillation of a mild silver nitrate solution, should not be started until about two weeks after the swelling in the epididymis and acute symptoms have subsided. This massage should not be vigorous at first and should be carried out at intervals of from five days to one week.

TREATMENT OF PITYRIASIS ROSEA

To the Editor:—What is the present accepted treatment for pityriasis rosea? Is ultraviolet radiation of any value in this condition? Please omit name.

M.D., Iowa.

ANSWER.—Pityriasis rosea is a self-limited disease, but in the majority of instances its course can be definitely shortened by the use of mild erythema exposures of ultraviolet rays at intervals of from five to seven days, plus soothing local treatment. The latter may consist of applications of calamine lotion, calamine liniment or boric acid ointment, or 5 per cent boric acid in rose water ointment. For scaling lesions, from 2 to 3 per cent salicylic acid may be added to the ointments.

EFFECTS OF MYDRIATICS

To the Editor:—An optometrist in this city is claiming that permanent blindness was caused in a case in which "drops" were used in the eyes, presumably homatropine or atropine 1 per cent. Is this possible? Please omit name.

M.D., North Carolina.

ANSWER.—Permanent blindness can follow the use of a mydriatic only in case glaucoma was present at the time of administration or some form of glaucoma resulted from the drops and did not receive or respond to adequate treatment. There are no recorded instances of blindness due to the use of a mydriatic without the intervention of increased intra-ocular pressure.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 29-July 1. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ALASKA: Juneau, March 2. Sec., Dr. W. W. Council, Juneau.

ARIZONA: Phoenix, Jan. 5-6. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: *Medical (Regular).* Little Rock, May 11-12. Sec., State Medical Board of the Arkansas Medical Society, Dr. A. S. Buchanan, Prescott. *Medical (Eclectic).* Little Rock, May 11. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Reciprocity.* San Francisco, Jan. 6. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, Jan. 5. Sec., Dr. Harvey W. Snyder, 422 State Office Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Feb. 13. *Prerequisite to license examination.* Address State Board of Healing Arts, 1895 Yale Station, New Haven. *Medical (Homeopathic).* Derby, Feb. 13. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven. *Medical (Regular).* Hartford, March 9-10. *Endorsement.* Hartford, March 23. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden.

DELAWARE: Dover, July 13-15. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, Dover.

DISTRICT OF COLUMBIA: Washington, Jan. 11-12. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

IDAHO: Boise, April 6. Commissioner of Law Enforcement, Hon. Emmitt Pfost, 205 State House, Boise.

ILLINOIS: Chicago, Jan. 26-28. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 22-24. Sec., Board of Medical Registration and Examination, Dr. William R. Davidson, 301 State House, Indianapolis.

IOWA: *Basic Science.* Des Moines, Jan. 12. Sec., Prof. Edward A. Benbrook, Iowa State College, Ames.

MAINE: Portland, March 9-10. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MICHIGAN: Ann Arbor and Detroit, June 9-11. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-3-4 Hollister Bldg., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, Jan. 5-6. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, Jan. 19-21. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MONTANA: Helena, April 6. Sec., Dr. S. A. Cooney, 7 W. 6th Ave., Helena.

NEBRASKA: *Basic Science.* Omaha, Jan. 12-13. Director, Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: *Reciprocity.* Carson City, Feb. 1. Sec., Dr. John E. Worden, Carson City.

NEW HAMPSHIRE: Concord, March 11-12. Sec., Board of Registration in Medicine, Dr. Charles Duncan, State House, Concord.

NEW JERSEY: Trenton, June 15-16. Sec., Dr. James J. McGuire, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 12-13. Sec., Dr. Le Grand Ward, Box 693, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 25-28. Chief, Professional Examinations Bureau, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH DAKOTA: Grand Forks, Jan. 5-8. Sec., Dr. G. M. Williamson, 4½ S. 3rd St., Grand Forks.

OREGON: Portland, Jan. 5-7. Sec., Dr. Joseph F. Wood, 509 Selling Bldg., Portland.

PENNSYLVANIA: Philadelphia, Jan. 5-9. Sec., Board of Medical Education and Licensure, Mr. James A. Newpher, Education Bldg., Harrisburg.

PUERTO RICO: San Juan, March 2. Sec., Dr. O. Costa Mandry, Box 536, San Juan.

RHODE ISLAND: Providence, Jan. 7-8. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Pierre, Jan. 19-20. Dir., Division of Medical Licensure, Dr. B. A. Dyar, Pierre.

VERMONT: Burlington, Feb. 10-12. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

WASHINGTON: *Basic Science.* Seattle, Jan. 7-8. *Medical.* Seattle, Jan. 11-13. Dir., Department of Licenses, Mr. Harry C. Huse, Olympia.

WEST VIRGINIA: Charleston, March 1. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: Madison, Jan. 12-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, Feb. 1. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Feb. 9-11, May 10-12, June 21-23, and Sept. 13-15. *Part III.* New York, Jan. 11-13 and Chicago, Jan. 19-21. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written examination for Group B applicants* will be held in various cities throughout the country, April 17. *Oral examinations for Group A and B applicants* will be given in Philadelphia, June 7-8. Sec., Dr. C. Guy Lane, 416 Marlborough St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written* examination will be held simultaneously in different centers of the United States and Canada in March. *Practical* examination will be given in St. Louis in April and at Philadelphia in June. Chairman, Dr. Walter L. Bierring, 406 Sixth Ave., Rm. 1210, Des Moines.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written examination for Group B applicants* will be held in various cities throughout the United States and Canada, March 6. *Practical, oral and clinical examinations for Group A and B applicants* will be held at Atlantic City, N. J., June 7-8. *Applications must be received at least sixty days prior to the examination dates.* Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: Los Angeles, Jan. 23. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis, Mo.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Cleveland, Jan. 9. Sec., Dr. Fremont A. Chandler, 180 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Philadelphia, June 7-8. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: Chicago, March 26-27. Sec., Dr. F. W. Hartman, Henry Ford Hosital, Detroit, Michigan.

AMERICAN BOARD OF PEDIATRICS: New York, Jan. 23. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Illinois.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 29-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Atlantic City, June 4-6. Sec., Dr. Byrl R. Kirklin, Mayo Clinic, Rochester.

Wisconsin June-July Report

Dr. Robert E. Flynn, former secretary, Wisconsin State Board of Medical Examiners, reports the written and practical examination held in Milwaukee, June 30-July 3. The examination covered 19 subjects and included 100 questions. An average of 75 per cent was required to pass. Ninety candidates were examined, 89 of whom passed and 1 failed. Thirty-one physicians were licensed by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1935)	82
Loyola University School of Medicine		(1932)	81
Northwestern University Medical School		(1935)	84, 84, 87, (1936) 82, 84, 84, 85
Rush Medical College		(1936)	81, 83, 85, 85, 86, 87
School of Medicine of the Division of the Biological Sciences		(1935)	84
University of Illinois College of Medicine		(1936)	82, 83, 86, 87
University of Louisville School of Medicine		(1935)	83
Tulane University of Louisiana School of Medicine		(1935)	79
Harvard University Medical School		(1927)	85
Washington University School of Medicine		(1935)	83
University of Pennsylvania School of Medicine		(1934)	86
Marquette University School of Medicine		(1935)	89, (1936) 77, 80, 80, 81, 81, 81, 81, 82, 82, 83, 83, 83, 83, 83, 83, 83, 83, 84, 84, 84, 85, 85, 85, 85, 85, 85, 86, 86, 86, 86, 86, 86, 87, 88, 89
University of Wisconsin Medical School		(1933)	83, (1935) 80, 81, 81, 81, 82, 82, 82, 83, 83, 83, 84, 84, 85, 85, 85, 86, 86, 86, 86, 86, 87, 88
Friedrich-Alexanders-Universität Medizinische Fakultät, Erlangen		(1923)*	87
Osteopaths†		83, 84,	88

School	FAILED	Year Grad.	Per Cent
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin		(1924)*	74

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical Evangelists		(1934)	California
Chicago Medical School		(1929)	Illinois
Loyola University School of Medicine		(1929), (1931), (1934)	Illinois
Northwestern University Medical School		(1929), (1930) (1930)	Illinois, Minnesota
Rush Medical College		(1933)	Illinois, (1934) California
Univ. of Illinois College of Medicine		(1933), (1934), (1935)	Illinois
University of Maryland School of Medicine and College of Physicians and Surgeons		(1916)	S. Carolina, (1930) Penna.
University of Michigan Medical School		(1930),	(1932) Michigan
University of Minnesota Medical School		(1930),	(1933, 2) Minnesota
Washington University School of Medicine		(1933)	Missouri
University of Nebraska College of Medicine		(1934)	Nebraska
Temple University School of Medicine		(1931)	Minnesota
University of Pennsylvania School of Medicine		(1923)	Penna.
Vanderbilt University School of Medicine		(1931)	Tennessee
Marquette University School of Medicine		(1934)	Minnesota
University of Wisconsin Medical School		(1934)	Penna.
Osteopaths†		Iowa, Missouri, New York,	South Dakota

* Verification of graduation in process.
† Licensed to practice osteopathy and surgery.

Missouri Reciprocity and Endorsement Report

Dr. E. T. McGaugh, state health commissioner, reports 22 physicians licensed by reciprocity and 5 physicians licensed by endorsement at the meeting held in Jefferson City, Aug. 11, 1936. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Howard University College of Medicine		(1932)	Maryland
Northwestern University Medical School		(1929)	Illinois
Indiana University School of Medicine		(1927)	W. Virginia
State University of Iowa College of Medicine		(1935)	Iowa
University of Kansas School of Medicine		(1931), (1932), (1933, 2), (1934, 2), (1935, 3)	Kansas
University of Louisville School of Medicine		(1935, 3)	Kentucky
Detroit College of Medicine and Surgery		(1933)	Michigan
University of Nebraska College of Medicine		(1935)	Nebraska
University of Cincinnati College of Medicine		(1936)	Ohio
University of Oklahoma School of Medicine		(1935)	Oklahoma
Jefferson Medical College of Philadelphia		(1923)	Penna.
University of Tennessee College of Medicine		(1933)	Tennessee

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Arkansas School of Medicine		(1935)	N. B. M. Ex.
Washington University School of Medicine		(1927), (1931), (1933)	N. B. M. Ex.
Meharry Medical College		(1934)	N. B. M. Ex.

Book Notices

A Text-Book of Neuro-Anatomy. By Albert Kuntz, Ph.D., M.D., Professor of Micro-Anatomy in St. Louis University School of Medicine. Second edition. Cloth. Price, $6. Pp. 519, with 307 illustrations. Philadelphia: Lea & Febiger, 1936.

This work has been thoroughly revised. The anatomic details are correlated with the fundamental structural plan of the vertebrate nervous system. The anatomic structure of the parts of the human nervous system are discussed in the light of the present knowledge of phylogenic, anatomic and physiologic relationships. There are twenty-six chapters, starting with evolution and comparative anatomy of the nervous system and concluding with a brief laboratory outline. Embryology, topography, histology, anatomy and physiology of the entire cerebrospinal, peripheral and autonomic nervous systems are clearly discussed and interpreted. The autonomic nervous system included in this book comprises material from the first five chapters of the author's book on the autonomic nervous system. The discussion of the cerebral hemispheres is brilliant because of its extreme comprehensiveness and clarity, and the ability to make interesting reading. In fact, the entire book is written in a concise and clear cut maner, thus making it a desirable textbook for students as well as for medical men interested in neurology. It is highly recommended.

Osnovy morfologii nervnoy sistemy v normalnom i patologicheskom sostoyaniyakh. Tom I: Obshchaya normalnaya i patologicheskaya gistologiya: gliya i mezoderma. [By] L. I. Smirnov. [Morphology of Nervous System in Normal and Pathologic Conditions. Volume I: General Normal and Pathologic Histology; Glia and Mesoderm.] Boards. Price, 18 rubles. Pp. 360, with 238 illustrations. Kharkov: Gosmedizdat Uk. S. S. R., 1935.

In a short preface the author states that in the Soviet Republics the interest in neuropathology has become of late so great that there is hardly a neuropsychiatric establishment without a properly equipped histopathologic laboratory. Psychiatric institutes are being gradually equipped with necropsy rooms, and the growing number of research neuropsychiatric centers attracts numerous young physicians eager to work in the field of pathology. In the introduction (thirty-six large pages of small print) the author enlarges on the importance of neuropathology in general, without the knowledge of which, he justly states, there can be no progress in the intelligent understanding of neuropsychiatric problems. Unfortunately, he did not spare efforts to exaggerate the shortcomings of neuropathology or to enlarge on the difficulties associated with its studies, such as the necessity of extensive clinical observations and of a previous training in anatomy, physiology, histology, embryology and other allied sciences. The picture painted by the author is so bewildering that the young men to help whom the book has been written may become discouraged from taking up the study of neuropathology. Even more discouraging is the mode of presenting the subject. Thus, while the book contains an immense amount of valuable information, the arrangement of the material is loose and therefore confusing Discussing glia, for instance, the author is not satisfied with a detailed general description of the various forms of glial elements and the methods of their study but does not hesitate to take up in detail the numerous morbid conditions (including gliomas) in which abnormal glia is encountered. It would be better to refer to the special volume and thus avoid repetitions, which are numerous. The author thinks it equally important to describe the condition of the glia found in an old dog or to discuss in four pages the minute types of granules occurring in glia. Even such topics as the nature and origin of rod cells do not require seven pages (including four pictures). On the

other hand, such an important subject as that of secondary nerve degeneration is given about half a page. The reading is rendered more difficult because of frequent quotations from the German and occasionally Russian medical literature. German quotations are so numerous that the impression is gained that one is reading the verbose contributions of Spielmeyer and Jakob, which are quoted with especial frequency. Non-German authors are mentioned only when their publications happened to appear in German, though the author gives the English caption of Cushing and Bailey's book on classification of gliomas (but this also appeared in a German translation). The book may be looked on as a review of or a compilation from German and Russian writings on various topics of neuropathology and for this reason may be of some help as a reference book. The illustrations, though numerous, are for the most part worthless because of the poor quality of the paper.

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1935, with the Comments that Have Appeared in The Journal. Cloth. Price, $1. Pp. 139. Chicago: American Medical Association, 1935.

The contents of the 1935 volume of collected reports of the Council fall roughly into three classifications: preliminary and special reports, reports on the omission of products from New and Nonofficial Remedies, and reports on products held nonacceptable for N. N. R. The medicinal products concerned thus fall respectively into the following groups: products which have been considered and found promising but not as yet fully acceptable, products which have been accepted but have not continued to meet the standards of acceptability, and products which on initial or continued consideration have been found definitely unacceptable. It is understood, of course, that the term "acceptable" implies that the product has sufficient value or promise of value to be used by the general medical profession and further that it is marketed in accordance with the Council's rules.

The Council's preliminary reports cover the first line of therapeutic advance. In general these reports give a review of the evidence for products representing the latest therapeutic investigation and indicate the procedure and requirements necessary for their ultimate admission to the physician's armamentarium. In this volume the report on progynon-B touches on the active and promising field of ovarian hormone therapy and the report on vitamin A and urinary lithiasis sets up a warning sign in the chaotic no man's land of overenthusiastic claims for vitamin therapy. An additional pronouncement in this field is found in the report on shotgun vitamin therapy. The Council is indeed to be commended for its rational stand in its attempt to clear up the mists of pseudoscience that have invaded this field.

The reports on articles omitted from New and Nonofficial Remedies usually give a parting notice to products on the way to the therapeutic scrap heap. The reports on lithium salts and tyramine hydrochloride are excellent examples of this type. The report on rossium, on a bacillus acidophilus culture and on dinitrophenol should also be noted as dealing with products that have been tried and found wanting.

It is significant that reports on products which on first examination are found flagrantly unacceptable comprise less and less of the bulk of the Council's work. They are represented in this volume by such reports as that on Elixir Aurine, an apparently uncontrolled mixture of gold tribromide and ephedrine for use in the treatment of whooping cough; Ho-Mo-Sol, a solution of sodium hypochlorite and sodium carbonate representing an unessential modification of a standard hypochlorite solution, marketed under a noninformative proprietary name and promoted to the public; the Imbak products, which are apparently bacterial preparations of undeclared composition, marketed with absurdly comprehensive claims, and Sulfoin, an ointment of solution of sulfuretted lime marketed under a proprietary name with inadequately supported therapeutic claims.

One is tempted to mention each one of the valuable reports included in this volume, but the limits of a review must be observed. Attention must, however, be called to the reports on omission from New and Nonofficial Remedies of Caprokol and Hexylresorcinol Solution S. T. 37 as illustrative of the judicial fairness and careful procedure of the Council on Pharmacy and Chemistry of the American Medical Association.

Les kystes hydatiques de la rate. Par L. Sabadini, chirurgien des hôpitaux d'Alger. Préface du Professeur Costantini. Paper. Price, 32 francs. Pp. 200, with 82 illustrations. Paris: Masson & Cie, 1936.

Sabadini's monograph on hydatid cysts of the spleen lives up to the tradition of the French school and the publishing house of Masson & Cie. In a clear and analytic manner the author goes into the greatest detail in his discussion of a lesion that is rare even in hydatid disease and seen only in regions where the ecchinococcus is endemic. In fact, Sabadini introduced his discussion of the subject by saying that only about 2 to 4 per cent of hydatid cysts become localized in the spleen. It is rarely reported from Iceland and Australia, being more commonly seen in Algiers and Italy. The chapters are on incidence, history, pathogenesis, pathology, symptomatology and signs, diagnosis and treatment. References are numerous throughout the monograph and it closes with a complete bibliography listing 288 articles and making the monograph desirable for this reason alone. The most valuable chapter by far is the one on treatment, which is subdivided under the headings of indications and operative procedures. The author clearly and logically brings out the complicating factors of enormous size, dangers of anaphylaxis, massive adhesions, dangers of spreading the parasites into the peritoneum and secondary infection, which have to be considered in the individual case in choosing marsupialization, removal of the cyst with primary closure or splenectomy. The indications and contraindications with the detailed technic are given clearly and succinctly. Coming from a surgeon of wide experience in Algerian hospitals, this chapter is noteworthy and adds an individual and personal note to the monograph with its complete bibliography.

A Diabetic Manual for Practitioners and Patients. By Edward L. Bortz, A.B., M.D., F.A.C.P., Associate Professor of Medicine, Graduate School of Medicine, University of Pennsylvania. With a foreword by George Morris Piersol, B.S., M.D., F.A.C.P., Professor of Medicine, Graduate School of Medicine, University of Pennsylvania. Fabrikoid. Price, $2. Pp. 222, with 12 illustrations. Philadelphia: F. A. Davis Company, 1936.

This little volume is intended both for the practitioner and for the patient, a combination that is always difficult to manage. It is bound to become too technical for the patient. Such a book, of which this is an example, contains too many technical terms that are foreign to a layman in spite of the glossary of medical terms at the beginning of the book. It contains too much that is neither of interest nor of use to the patient and tends to confuse him rather than to clarify the problem for him. From the standpoint of the patient therefore it is top heavy. From the standpoint of the practitioner, it is an excellent little volume, full of practical type of information. Any one in busy practice will find a good guide here in the treatment, diagnosis and complications of diabetes. In the chapter on diet the author has used a new and simple method of measuring in place of the usual weighing of the food, which is a practical and helpful method as it simplifies the routine and is adequate for all practical purposes. The chapter on food analysis and recipes follows much the usual lines and to this are added lists of the composition of alcoholic beverages, a helpful feature for reference.

An Introduction to Surgery. By Rutherford Morison, M.D., F.R.C.S., M.A., and Charles F. M. Saint, C.B.E., M.D., M.S., Professor of Surgery, Cape Town University, South Africa. Third edition. Cloth. Price, $5. Pp. 367, with 231 illustrations. Baltimore: William Wood & Company, 1935.

This rather small volume is devoted to the establishment of general principles as applied to the teaching of surgery. The authors point out that deviations from normal health are due to changes in the body caused by external or internal stimuli, which may be divided into two main groups: noninfective—mechanical, thermal, chemical, electrical, x-ray—and infective. A proper understanding of surgery consists in an understanding of how these harmful stimuli or irritants affect the body and how nature overcomes these changes. These facts constitute the general principles and the authors in this textbook are concerned with the presentation of these principles and their constant, forceful repetition and illustration by cases. The volume is not a complete textbook of surgery. The subjects taken up include shock, hemorrhage, infection, inflammation, wounds, inflammatory fever, effects of interference with blood supply

of tissues, suppuration, specific infectious diseases, ulcers, gangrene, syphilis, tuberculosis, malignant disease, the hollow muscular systems, the serous cavities, natural cures and indications for operation. It ends with a chapter on pathologic conditions illustrating the principles of surgery: consideration of etiology, pathology, symptomatology, diagnosis and treatment. The work contains nothing that is essentially new and it could not be used as a textbook on general surgery, it is so incomplete; but it must have been found of value to warrant its third edition. The authors are men of large experience and high standing, and their manner of presenting surgical principles is interesting and valuable. Their aim and their achievements are to aid the student in thinking out for himself the problems presented to him clinically and in textbooks, placing each problem in a general group rather than considering it as an isolated entity. Once the student has gained such a point of view, he ceases to be overwhelmed by the mass facts presented to him, thinks systematically and logically, and finds greater interest in the subjects.

The Therapeutic Agents of the Pyrrole and Pyridine Group Including the Tropinol, Scopoline, Ecgonine, and Granatoline Derivatives. The Relation Between Their Chemical Constitution and Pharmacologic Action. By W. F. von Oettingen, M.D., Ph.D., Director of the Haskell Laboratory of Industrial Toxicology, Wilmington, Delaware. Cloth. Price, $4.75. Pp. 258. Ann Arbor, Michigan: Edwards Brothers, Inc., 1936.

This volume is a real contribution to scientific literature because it represents a collection of chemical and pharmacologic data on several series of nitrogen-containing organic compounds. The subtitle on the fly leaf indicates that the volume discusses "The Relation Between Their Chemical Constitution and Pharmacologic Action." Unfortunately, this is not the case. In the last paragraph the author indicates that he recognizes no such relationship, but he suggests that the relationship may be established when a greater fund of knowledge of physicochemical properties and reactions is at hand.

The chemistry consists in giving the names of the compounds according to *Chemical Abstracts* nomenclature, portraying the structural formulas, which are given in great effusion and without arguments for or against, and for some compounds a few physical properties. Methods of isolation and preparation are not given. The volume would be more valuable to the chemist if the chemical data were more complete. The pharmacologic data are more complete than the chemical and are necessarily factual in nature. It must be pointed out that the size of the volume would soon get out of control if these subjects were treated more completely. From the pharmacologist's point of view the bibliography is excellent; from the chemist's it is incomplete. This volume and Die Chemie des Pyrrols by Dr. Hans Fischer and Dr. H. Orth would be complemental, as the one deals with pharmacology and the other with chemistry.

The format of the book will be welcomed. The printing process is photolithograph on a not too expensive paper. The binding appears to be well done but again with inexpensive materials. In this economical setup the printing is very legible, being clear, large and not crowded and, in addition, structural formulas and tables are not spared. Many scientifically valuable books may become financially possible if some such economical format becomes accepted.

Pathology of the Nervous System: A Student's Introduction. By J. Henry Biggart, M.D., Pathologist to the Scottish Asylums' Board. Foreword by Professor A. Murray Drennan, M.D., F.R.C.P. Cloth. Price, $5.25. Pp. 335, with 204 illustrations. Baltimore: William Wood & Company, 1936.

This is written clearly and briefly and yet includes almost every entity one deals with in neuropathology. The author has succeeded in keeping together the relationship of the etiology to the pathology of each disease described. There is also a closer correlation between general pathology and the pathology of the nervous system than is found in most textbooks. The illustrations are excellent. The book is divided into fourteen chapters, on the nerve cells, the interstitial cells, the cerebrospinal fluid, vascular disease and the brain, acute bacterial infections, chronic infections, virus diseases, diseases of unknown etiology, intoxication and deficiency diseases, degenerative diseases, injuries to the nervous system, tumors of the glioma group, and errors in development. There is a small bibliography, but the works mentioned are in the English language. This book is recommended to medical students as well as to those interested in the pathology of the central nervous system.

Grundriss der inneren Medizin. Von A. von Domarus, a. o. Professor an der Universität Berlin. Tenth edition. Cloth. Price, 16.80 marks. Pp. 681, with 63 illustrations. Berlin: Julius Springer, 1936.

The first edition of this textbook of internal medicine appeared in 1923. The author is a pupil of the clinician and teacher Friedrich Müller. He has written this book on internal medicine as a guide to the young physician and medical student. He devotes 130 pages to the infectious diseases. Then follow circulatory diseases (seventy-three pages), respiratory diseases (sixty pages), blood diseases (twenty-five pages), diseases of the digestive tract (112 pages), of the urinary tract (fifty-two pages) and of the ductless glands (twenty pages), metabolic diseases (forty-eight pages) and diseases of the locomotor apparatus (twelve pages) and the nervous system (124 pages). The book has more information than most textbooks of its size, as a considerable portion is printed in small type. Some of the illustrations are in colors. The textbook is an excellent and concise outline of our present knowledge of internal diseases.

Bailey's Text-Book of Histology (Elwyn and Strong). Revised and rewritten by Philip E. Smith, Ph.D., Editor, Professor of Anatomy, College of Physicians and Surgeons, Columbia University, and others. Ninth edition. Cloth. Price, $6. Pp. 773, with 506 illustrations. Baltimore: William Wood & Company, 1936.

The present revision is a cooperative undertaking of five members of the Anatomy Department of Columbia University College of Physicians and Surgeons. They have kept before them the fundamental idea that this was to be a textbook for students rather than a source book for teachers and research workers. They have endeavored to discuss the physiologic significance of the numerous structures described. The various revisers were assigned to those chapters in which they are most interested. The chapter on the central nervous system, written by Dr. Oliver Strong, which was revised in the last edition, remains unchanged. Some chapters have been entirely rewritten and many others have been brought down to date. This edition is well illustrated and a few of the illustrations are in colors.

Experimental Enzyme Chemistry. By Henry Tauber, Ph.D., New York Homeopathic Medical College and Flower Hospital, New York, N. Y. Fabrikoid. Price, $3.50. Pp. 118. Minneapolis: Burgess Publishing Company, 1936.

This volume includes a number of highly technical essays on the chemistry of the enzymes under the following chapter headings: Physical Chemistry of the Enzymes; Esterases; Proteolytic Enzymes and Peptidases, Mammal Gastric Proteases, Tryptases, Peptidases; Amidases; Carbohydrases, Sucrase (Saccharase, Invertase), Glucosidases, Maltases, Galactosidases, Lactase, Melibiase, "Emulsion," Polyases, Lichenase, Cellulase, Inulase; Catalase; Oxidizing Enzymes, Dehydrogenases or Anaerobic Oxidases, Oxidases or Aerobic Oxidases; The Flavine Oxidation System of Warburg and Christian and Its Relation to Other Dyes; Carbonic Anhydrase; The Zymase Complex and Alcoholic Fermentation; Luciferase. For all those interested in research in this field, it may be of special value; for the general reader, it is, of course, a book of reference.

Über die Ursache und Entstehung des Krebses: Zugleich eine Anleitung zur Erschliessung des Zellbildes bösartiger Geschwülste. Von Prof. Dr. med. Jos. Koch. Paper. Price, 32 marks. Pp. 302, with 32 illustrations. Jena: Gustav Fischer, 1936.

This monograph summarizes the results of Koch and his pupils on the protozoic etiology of cancer. Based on the examination of 260 human cancers and on transplantable animal cancers, he concludes that cancer is due to a protozoic organism, "cellula cancrosa specifica s. parasitoia," which enters through the intestinal and female genital tracts. "All phenomena in carcinoma, as manifold as they may be, can be related easily to one cause: the presence of the parasitic cell, and they can be satisfactorily explained by this." He discusses extensively the objections which have already been made in the literature and which, in most instances, are based on the conception of the wrong interpretation of degenerated products in cancer material, as parasitic specific cells. "To the chaos of

indecisive opinions and uncertain imaginations, I oppose my interpretation, which is able to relate the cytologic pictures to a uniform cause, namely, the existence of an exogenic protozoic cell parasite, and to interpret the pictures completely." In spite of the great amount of work and the excellent microscopic pictures (mostly colored), this book, written perhaps with honest enthusiasm but certainly without scientific criticism, will not solve the problem of the etiology of cancer. It particularly does not add any new information to further the still unsettled question of a relationship of living organisms to carcinogenesis.

Exercises After Delivery or Operation. By Walter B. Mount, M.D., Obstetrical Department, Mountainside Hospital, Montclair, N. J. Paper. Pp. 6, with illustrations. Privately printed, 1935.

In this booklet the author describes and illustrates a few conventional exercises for patients to take shortly after a delivery or operation. He promises his patients who carry out these exercises faithfully that they will the sooner regain their girlish figure.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Hospital Records as Privileged Communications.—The defendant insurance company issued in April 1932 a policy on Vermillion's life, which was not to take effect if on the date of its delivery the insured was not in sound health. Vermillion died Nov. 14, 1932. When his beneficiary brought suit on the policy the company denied liability, claiming that at the time of the delivery of the policy the insured was "suffering from latent syphilis, chronic heart disease, swelling ankles, lues, nephritis, shortness of breath, cough frequency, and nocturia, and had been suffering from said ailments and was under the care of physicians for a long time prior" thereto and that as a result thereof the insured died of "heart disease and syphilis." To prove this it sought to introduce into evidence a case history made when the insured was admitted to a hospital about seven weeks after the delivery of the policy. The trial court excluded the hospital records proffered. Judgment was subsequently rendered in favor of the beneficiary and the insurance company appealed to the St. Louis (Missouri) court of appeals.

The defendant contended that the hospital records sought to be admitted in the trial court were admissible in evidence because they were kept in compliance with a Missouri statute (sec. 9056, R. S. Mo. 1929), requiring persons in charge of hospitals, public or private, to make a record of all the personal and statistical particulars relative to the inmates in their institutions. There is no doubt, answered the court of appeals, that hospital records, properly identified and shown to be kept pursuant to this statute, are admissible in evidence. However, the admissibility of such records may be affected by another statute (sec. 1731, R. S. Mo. 1929), which provides that a physician or surgeon shall be incompetent to testify "concerning any information which he may have acquired from any patient while attending him in a professional character, and which information was necessary to enable him to prescribe for such patient as a physician, or do any act for him as a surgeon." The defendant argued, however, that the trial court was not justified in assuming that the records were privileged merely on the assertion of counsel for the plaintiff that the information contained in those records was privileged and without proof of any kind being offered in support of that assertion.

It is true, said the court, that the mere assertion of the privilege, without any showing of facts or circumstances from which the court can determine the necessity for the application of the statute under which the privilege is claimed, is not sufficient to warrant a court in rejecting the proffered evidence or testimony. Nor is the mere relationship of physician and patient alone sufficient to warrant a court in rejecting, on the ground of privilege, evidence which would otherwise be competent. In the present case, however, the relationship of physician and patient and the fact that the information contained in the case history was obtained by virtue of that relationship were sufficiently shown on the face of the case history itself to warrant the court in excluding it as a privileged communication. While it is true that the first page of the case history is not signed by any physician, such a signature was not necessary as a basis for the claim of privilege. The entries constituted a prima facie showing that the information was of a confidential and privileged character. If, as claimed by the insurance company, such information was not given by the patient to the hospital physicians for the purpose of enabling them to prescribe for the patient, then the burden was on the insurance company to produce evidence to satisfy the court to that effect and to overcome the prima facie showing of the confidential character of the information appearing therein.

In Missouri, continued the court of appeals, hospital records containing information obtained by a physician from a patient for the purpose of enabling him to treat or prescribe for the patient are as fully privileged as would be the testimony of the physician himself concerning such information, provided the privilege has not been waived by the party asserting it. The court was of opinion that the evidence contained in the case history was of a confidential nature acquired from the patient by the physician in charge of the hospital, or by physicians acting for him, for the purpose of enabling such physicians to treat the patient in the hospital, and that the trial court was warranted in rejecting such evidence. The judgment in favor of the beneficiary was accordingly affirmed.—*Vermillion v. Prudential Ins. Co. of America (Mo.), 93 S. W. (2d) 45.*

Workmen's Compensation Acts: Pneumonia Not an "Injury by Accident."—Slade, after working indoors in an exceedingly hot environment, made several trips outdoors. That evening he became ill and on the following day his attending physician made a diagnosis of "consolidated pneumonia," which the physician testified was "due to sudden change of temperature, going from the hot room out into the open air. It produced a congestive chill." Slade died six days later and his widow instituted proceedings under the North Carolina workmen's compensation act. An award of compensation made by the industrial commission in her favor was reversed by the superior court, Cabarrus county, and the widow appealed to the Supreme Court of North Carolina.

The North Carolina workmen's compensation act, said the Supreme Court, provides compensation for death only where death results from an injury by accident arising out of and in the course of the employment. Death from injury by accident implies a result produced by a fortuitous cause. In the present case, said the court, there was no evidence of any accidental injury arising out of and in the course of employment which resulted in the death of the employee. Compensation was therefore properly denied the widow.—*Slade v. Willis Hosiery Mills (N. C.), 184 S. E. 844.*

Society Proceedings

COMING MEETINGS

American Academy of Orthopedic Surgeons, Cleveland, Jan. 11-13. Dr. Philip Lewin, 55 East Washington St., Chicago, Secretary.

American Orthopsychiatric Association, New York, Feb. 18-20. Dr. George S. Stevenson, 50 West 50th St., New York, Secretary.

Annual Congress on Medical Education, Medical Licensure and Hospitals, Chicago, Feb. 15-16. Dr. William D. Cutter, 535 North Dearborn St., Chicago, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Boston, Jan. 7. Dr. D. C. Jarvis, Quarry Bank Bldg., Barre, Vt., Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Chicago, Jan. 11. Dr. Alfred Lewy, 25 East Washington St., Chicago, Chairman.

Mid-Western Section, American Laryngological, Rhinological and Otological Society, Chicago, Jan. 11. Dr. Frederick A. Figi, 436 Tenth Ave. S.W., Rochester, Minn., Chairman.

Society of American Bacteriologists, Indianapolis, Dec. 28-30. Dr. I. L. Baldwin, College of Agriculture, University of Wisconsin, Madison, Wis., Secretary.

Society of Surgeons of New Jersey, Newark, Jan. 6. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.

Southern Section, American Laryngological, Rhinological and Otological Society, Memphis, Tenn., Jan. 13. Dr. Charles D. Blassingame, Physicians and Surgeons Bldg., Memphis, Tenn., Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, San Diego, Calif., Jan. 30-31. Dr. David R. Higbee, 3245 Fourth Ave., San Diego, Calif., Chairman.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers in continental United States and Canada for a period of three days. Periodicals are available from 1926 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

California and Western Medicine, San Francisco

45: 305-376 (Oct.) 1936

Tumors and Cysts of Lung: Diagnostic Methods. J. J. Singer, St. Louis.—p. 313.

Medical Survey of One Thousand Work Relief Persons: Certified for Work Relief in San Francisco: Period Oct. 2 to 19, 1935. A. E. Larsen, San Francisco.—p. 317.

Mapharsen: Its Use in Treatment of Syphilis. H. E. Miller, N. N. Epstein and R. G. Simpson, San Francisco.—p. 321.

*Portal Thrombosis. E. C. Pallette, Los Angeles.—p. 324.

Obstetric Anesthesia. La Verne Wright, San Francisco.—p. 328.

Tests for Vasomotor Control. L. K. Gay and J. T. Hardesty, San Francisco.—p. 331.

Hypertension: Its Surgical Approach. F. M. Findlay, Santa Barbara. —p. 334.

Medical Management of Peptic Ulcer. G. A. Cochran, Salt Lake City. —p. 340.

Irritant Factors in Tobacco Smoke. E. Bogen, Olive View.—p. 342.

*New Sign Found in Transverse Lesions of Spinal Cord. W. J. Kerr and C. A. Noble Jr., San Francisco.—p. 346.

Meditations on Some Present-Day Medical Problems. A. C. Siefert, Oakland.—p. 348.

The Management of Alcoholism. H. H. Wilson, Los Angeles.—p. 349.

Portal Thrombosis.—Pallette discusses thrombosis of the portal venous system from the standpoint of etiology, symptomatology, frequency, pathologic physiology and treatment. The condition is too infrequently recognized as a clinical entity. The acute condition may closely simulate an abdominal emergency, and in the chronic form the associated splenomegaly should not be regarded as successfully amenable to surgical treatment. Unfortunately there is no treatment of any essential value in this condition. In acute cases the usual procedures for the treatment of shock, ileus and the like are instituted. In his own case the author felt that perhaps the repeated injections of intraspinal procaine hydrochloride given in the hope of relieving the marked ileus present was of considerable value and perhaps definitely influenced the outcome toward recovery. The basis for this opinion is that, in relieving the critical distention of involved intestine, the already embarrassed circulation to that loop is relieved. The huge ascites can be controlled by paracentesis. In the chronic cases, instructions should be given as to the avoidance of all alcoholic beverages or of any drug toxic in any way to the liver.

New Sign in Transverse Lesions of Spinal Cord.—In 1930 Kerr first noticed in a patient with a somatic sensory level due to a probable cord tumor that there was a change of the skin that could be felt. The skin above this level, which may be designated as normal, felt smooth, soft, moist and pliable and could be readily lifted between the thumb and forefinger. On the other hand, the skin below the level seemed stiff, "hide bound," dry and adherent to the subcutaneous layers, so that only with difficulty could a layer of skin be pinched together. It was found that this change could be sensed also by gently trying, with the tips of the extended fingers, to displace a segment of skin on its underlying tissues. Sometimes in patients studied subsequently the transition from normal to altered skin was abrupt, sometimes more gradual over one or two segments. Since 1930 Kerr and Noble have examined about 100 patients in the University of California Hospital and the San Francisco Hospital. The patient was usually in ignorance of the presence of any such level. Sixty-four subjects were examined presumably as normal controls. There were twenty patients with a somatic sensory level and other convincing evidence of disease of the spinal cord. Their diagnoses included both intramedullary and extramedullary tumors, transverse myelitis of degenerative or inflammatory origin, diffuse arachnoiditis and fracture of the spine. In these patients a level of skin tension was found which was in fairly close agreement, either with that somatic sensory level or, more often, with a level of change in sweating or pilomotor response. In ten of these twenty patients the level of the process in the cord was confirmed by operation or necropsy or, in the case of spinal fracture, by roentgen examination. In nine of these ten the level of skin tension corresponded exactly with the area of disease and in one case pointed to a tumor five segments higher in the cord than indicated by the somatic sensory level. In this patient, whose first laminectomy had ended in a fruitless search for the lesion, operation confirmed the suggestion of a higher level of skin tension. In ten patients with evidence of disease of the spinal cord with a somatic sensory level, no level of skin tension could be demonstrated. That this sign might affect the halves of the body differently is shown by two patients. In one of these patients there was a unilateral hypertonus of the skin associated with marked constriction of the peripheral vessels on the same side, secondary to a cerebral lesion in the opposite hemisphere. A similar observation was made in a patient with a nearly complete Brown-Séquard syndrome due to a fracture of the cervical spine.

Colorado Medicine, Denver

33: 737-856 (Nov.) 1936

The Syphilis Problem: How Shall We Meet It? H. N. Cole, Cleveland. —p. 750.

Protamine Insulinate at Colorado General Hospital: Clinical and Experimental Investigations. J. J. Waring, B. B. Longwell and A. Ravin, Denver.—p. 757.

Forty Years of Progress in Medicine. J. L. Wicks, Evanston, Wyo. —p. 821.

Iowa State Medical Society Journal, Des Moines

26: 549-602 (Oct.) 1936

Meningitis. A. L. Hoyne, Chicago.—p. 549.

*Mandelic Acid in Treatment of Bacilluria: Its Advantages Over Ketogenic Diet. B. G. Budge, Ames.—p. 553.

Injection Treatment of Hernia. C. H. Johnston, Des Moines.—p. 556.

Regional (Distal) Ileitis. F. W. Mulsow, Cedar Rapids.—p. 561.

The Woman Physician in a Changing World. Florence Brown Sherbon, Lawrence, Kan.—p. 564.

Study of 198 Cases of Female Genital Malignant Tumors. J. H. Randall, Iowa City.—p. 567.

Use of Trichloroacetic Acid to Obliterate Bleeding Points on Nasal Septum. F. G. Murphy, Mason City.—p. 571.

Encephalography in Children. Charlotte Fisk, Iowa City.—p. 572.

Lymphogranuloma Inguinale. L. J. Dimsdale, Sioux City.—p. 574.

26: 603-664 (Nov.) 1936

Recent Advances in Diagnosis and Treatment of Vulvovaginal Discharges (Bloodless). H. C. Hesseltine, Chicago.—p. 603.

Some Observations on Third Antigen of Bacillus Typhosus. W. J. Moore, Iowa City.—p. 610.

Rocky Mountain Spotted Fever. F. Montz, Lowden.—p. 614.

Some Factors in the Management of the Failing Heart. A. G. Felter, Van Meter.—p. 617.

Fractures of Vertebra. V. A. Ruth, Des Moines.—p. 620.

Modern Trends in Psychoneurotic Reaction Types. W. Malamud, Iowa City.—p. 625.

Refinements in Refraction. F. W. Dean, Council Bluffs.—p. 632.

Improved Mechanics in Maggot Therapy. J. J. Duffy, Denison.—p. 636.

Mandelic Acid in Treatment of Bacilluria.—From July 1935 to September 1936 Budge has treated forty-six cases of bacilluria with mandelic acid and ammonium chloride with such satisfactory results that the ketogenic diet has been discontinued. There has been one known recurrence in a young woman who discontinued treatment against instructions. In a man, aged 43, there was the severe complication of hemorrhage with acute retention, probably from the false passage of a sound in an attempt to dilate a stricture; however, he was relieved of symptoms. With mandelic acid, as with the ketogenic diet, best results are obtained with a highly acid urine. Mandelic acid is readily taken and well tolerated by children. Success with the ketogenic diet in children can rarely be attained in the home. It is not necessary to hospitalize a child to administer mandelic acid. The standardized ketogenic diet can be readily prepared in any home; the patient when away must depend on eggs and 40 per cent cream, but mandelic acid can be carried in the grip. The patient who is placed on the ketogenic diet is told that he may expect to become sick on the second day and often it is necessary to stop the diet temporarily because of persistent nausea. The longer mandelic acid is taken, the better it is tolerated. The ketogenic diet is contraindicated in diabetes, angina, biliary tract disturbances and in elderly people with arteriosclerosis, but mandelic acid can be used in these conditions.

Journal of Biological Chemistry, Baltimore

115: 593-808 (Oct.) 1936

Proteolytic Enzymes: XI. Specificity of Enzyme Papain Peptidase I. M. Bergmann, L. Zervas and J. S. Fruton, New York.—p. 593.
Origin of Urinary Creatinine. A. Goudsmit Jr., New York.—p. 613.
Glycogen Disappearance and Carbohydrate Oxidation in Hypophysectomized Rats. R. E. Fisher, St. Louis; Jane A. Russell, and C. F. Cori, St. Louis.—p. 627.
Deuterium as Indicator in Study of Intermediary Metabolism: VII. Studies in Bile Acid Formation. R. Schoenheimer, D. Rittenberg, B. N. Berg and L. Rousselot, New York.—p. 635.
Comparison of Glycine and Guanidoacetic Acid as Precursors of Creatine. M. Bodansky, with technical assistance of Virginia B. Duff and C. L. Herrmann, Galveston, Texas.—p. 641.
Partition of Reduced Ascorbic Acid in Blood. D. J. Stephens and Estelle E. Hawley, Rochester, N. Y.—p. 653.
Additional Observations on Anemia Caused by Deaminized Casein. A. G. Hogan, R. E. Guerrant and W. S. Ritchie, Columbia, Mo.—p. 659.
Chemical Studies on Virus of Tobacco Mosaic: VII. Improved Method for Preparation of Crystalline Tobacco Mosaic Virus Protein. W. M. Stanley, Princeton, N. J.—p. 673.
Further Studies on Calcium Content of Body in Relation to Calcium and Phosphorus Content of Food. L. B. Whitcher, Lela E. Booher and H. C. Sherman, New York.—p. 679.
Effect of Liberal Intakes of Calcium or Calcium and Phosphorus on Growth and Body Calcium. E. W. Toepfer and H. C. Sherman, New York.—p. 685.
Some Aspects of Protein Intake in Relation to Growth and Rate of Calcification. R. T. Conner and H. C. Sherman, New York.—p. 695.
New Essential Dietary Factor. C. A. Elvehjem, C. J. Koehn Jr. and J. J. Oleson, Madison, Wis.—p. 707.
Spatial Configuration of α-Amino-β-Hydroxy-n-Butyric Acid. C. E. Meyer and W. C. Rose, Urbana, Ill.—p. 721.
Improved Method for Preparation of Xylulose and Ribulose. P. A. Levene and R. S. Tipson, New York.—p. 731.
Effect of Dinitrophenol on Metabolism of Frog Muscle. Ethel Ronzoni and Ellen Ehrenfest, St. Louis.—p. 749.
Remarks on Paper by Tendeloo on New and Easy Method for Potentiometric Determination of Calcium Concentrations in Solutions. D. M. Greenberg and C. E. Larson, Berkeley, Calif.—p. 769.
Further Observations on Chemical Nature of Hematopoietic Substance Occurring in Liver. H. D. Dakin, New York; C. C. Ungley, Newcastle-on-Tyne, England, and R. West, Scarborough-on-Hudson, N. Y.—p. 771.

Laryngoscope, St. Louis

46: 731-814 (Oct.) 1936

Genetics in Otosclerosis. Helen F. Schick and M. A. Goldstein, St. Louis.—p. 731.
Selection and Operation of Audiometers. E. G. Witting, Abington, Pa.—p. 747.
Maxillary Sinusitis with Complicating, Spreading Osteomyelitis, Brain Abscess and Death: Report of Case. A. N. Lemon, Philadelphia.—p. 754.
Lingual Thyroid. L. T. Buckman, Wilkes-Barre, Pa.—p. 765.
Tuberculosis Associated with Esophageal Obstruction. H. P. Mosher, Boston.—p. 785.
*Suggested Routine Technic for Emergency Tracheotomy. W. B. Chamberlin, Cleveland.—p. 800.

Technic for Emergency Tracheotomy.—Chamberlin declares that the Mosher tube answers the problem of relief of sudden and acute laryngeal obstruction. Its ease of introduction in either the erect or the reclining posture leaves nothing to be desired, while its lumen gives ample space for free respiration while the tracheotomy is being performed. The technic in the main is the same as that used in the introduction of an intubation tube, except that there is no introducer to be removed. The forefinger of the left hand is carried over the base of the tongue until the tip of the epiglottis is felt. In children it is much better to feel for the arytenoids, which are distinguished as two small lumps on the flexor surface of the index finger. This prevents the tube from slipping into the esophagus. The tube is carried along the flexor surface of the index finger until its point is directly above the opening of the larynx. The handle or proximal end is elevated and the tip, guided by the finger, is pushed gently through the larynx and into the trachea. After the tube has been introduced, it is held in position by a nurse or assistant to see that it is neither coughed out nor displaced. The patient is then placed in the usual position for the tracheotomy. Before the trachea is opened, all bleeding is carefully controlled and the field inspected to see that it is perfectly dry. The trachea is opened either between the rings or by cutting directly across one of them. In older patients in whom larger tubes are used it is generally advisable to resect a portion of the ring to prevent undue pressure from the tube. This piece should be firmly grasped with forceps or hemostat to prevent aspiration. A blunt hook is then inserted through the opening and the trachea is drawn slightly upward. When the trachea is opened the convex surface of the Mosher tube, rather than the end, is usually brought into view. The tube is slightly withdrawn until the end appears above the first hook. Two other hooks are inserted, one on each side, and the tracheotomy tube is placed in position and firmly tied behind the neck. Two or more skin sutures may be necessary; also a small drain immediately above and below the tube to take care of superficial and late bleeding. The Mosher tube is then withdrawn.

Medical Annals of District of Columbia, Washington

5: 287-322 (Oct.) 1936

Constitutional Factors in Mental Disorders. W. Freeman, Washington.—p. 287.
*Traumatic Epilepsy with Cortical Scar: Diagnosis and Results of Operation in Twenty Cases. S. N. Rowe, Philadelphia, and J. W. Watts, Washington.—p. 298.
New York City Plans for Combating Syphilis. C. W. Clarke, New York.—p. 301.
Tuberculosis of Larynx. R. Reynolds, Washington.—p. 306.
William Cline Borden (1858-1934). D. L. Borden, Washington.—p. 310.

Traumatic Epilepsy with Cortical Scar.—Rowe and Watts relate the diagnostic features of their twenty cases of traumatic epilepsy with a cortical scar. All the patients had received severe head injuries prior to the onset of epilepsy. There was loss of consciousness for many hours and often for many days. Emergency operations for elevation of depressed fractures and débridement had been performed in several instances. Bone defects, obvious both from clinical and from roentgen examination, were present in 65 per cent of the patients. Laceration of the dura was found at operation in 35 per cent. Focal features of the convulsive seizures were observed in 60 per cent of the patients. Neurologic signs indicative of focal cerebral damage were present in 85 per cent. These varied from slight defects in the visual fields to partial hemiparesis. Of the fifteen patients in whom encephalograms were made, observations indicative of cerebral cicatrix were present in thirteen. There was an interval of fourteen years in two of the patients between the injury and the first convulsion, of thirteen years in one patient and of twelve years in another. The shortest period between injury and the first attack was three months and the next shortest was seven months. Excision of the cortical scar resulted in only slight, temporary or no improvement in 35 per cent of the patients, whereas 15 per cent were entirely relieved of attacks, and an additional 50 per cent showed marked improvement. The fact that 65 per cent of the patients were definitely benefited seems to justify removal of the cortical scar in attacking what is otherwise a hopeless condition.

Military Surgeon, Washington, D. C.

79: 341-422 (Nov.) 1936

The United States Army Medical Department 1861 to 1865. F. B. Ryons.—p. 341.
Partial List of Medical Men in the Maritime Service of Colonies During the American Revolution. L. H. Roddis.—p. 357.
Outbreak of Typhoid Fever in Camp of Civilian Conservation Corps. A. N. Tasker.—p. 358.
Mess Economy. J. W. Shuman.—p. 362.
Why the Flight Surgeon? W. S. Jensen.—p. 367.
The Surgical Hospital. L. E. Hetrick, New York.—p. 372.
Spontaneous, Intraperitoneal Rupture of Urinary Bladder with Recovery: Case. J. Bethea, A. P. Kelly and R. E. Bitner.—p. 379.
Dissemination of Cholera by the 38th Infantry in 1867. G. F. Lull.—p. 382.
Carbon Monoxide Poisoning. H. T. Berwald.—p. 386.
Method of Initiating Pneumothorax in the Tropics. R. B. Skinner.—p. 396.

New England Journal of Medicine, Boston

215: 693-742 (Oct. 15) 1936

Relationship of Psychiatry to Medicine. W. A. Bryan, Worcester, Mass.—p. 693.
Blood Iodine Level, Before and After Subtotal Thyroidectomy for Hyperthyroidism. H. J. Perkin and L. M. Hurxthal, Boston.—p. 698.
Acute Gastro-Intestinal Disease in Infants. R. M. Smith, Boston.—p. 701.
Surgical Diseases of Alimentary Tract in Infants. W. E. Ladd, Boston.—p. 705.
Diuretics and What They Do. H. A. Christian, Boston.—p. 709.
Progress in Gastro-Enterology for 1935. E. S. Emery Jr., Boston.—p. 712.

Pennsylvania Medical Journal, Harrisburg

40: 1-62 (Oct.) 1936

A Charge to Keep: Presidential Address. M. Lick, Erie.—p. 1.
Recognition of Therapeutic Use of Oxygen by Dr. George E. Holtzapple. C. M. Byrnes, Baltimore.—p. 8.
Treatment of Primary Hydrocele by Injection of Sodium Morrhuate. E. S. Krug, McConnellsburg.—p. 9.
Modern Dietetics in Disorders of Kidney and Genito-Urinary Tract. R. S. Reeves, Philadelphia.—p. 10.
*Clinical Significance of Hoarseness. A. J. Wagers, Philadelphia.—p. 14.
Chronic Compression of the Heart: By One Who Had This Condition. V. P. Pisula, Everson.—p. 18.
Peanut in Lung with Severe Complications: Report of Case. J. G. Koshland, Lewistown.—p. 20.
Medical Aspects of Social Hygiene in Montgomery County, Pa. R. A. Vonderlehr, Lida J. Usilton, Washington, D. C., and Helen Cole Carter, Norristown.—p. 21.

Clinical Significance of Hoarseness.—Wagers admonishes that hoarseness, particularly if unaccompanied by pain or a cough, is too often ignored by the patient and sometimes by the physician as well until such time as other and more alarming symptoms appear. Every case of hoarseness does not indicate a grave constitutional disease. But no matter how trivial the appearance of hoarseness may seem, it should always be regarded seriously. The immediate cause of hoarseness is found in various conditions affecting the proper functioning of the vocal cords. It becomes then the problem of the laryngologist to discover the immediate and if possible the remote or constitutional cause underlying and responsible for the local laryngeal manifestation. In all cases a careful and complete history should be the basis of the investigation, followed by inspection of the larynx, physical examination of the chest, roentgen study of the chest and the larynx, Wassermann test, and in certain instances microscopic study of removed laryngeal tissue. Frequently hoarseness or some other voice change is one of the first signs of pulmonary tuberculosis. Hoarseness may be and often is the first symptom indicating malignant invasion of the larynx. Nonmalignant neoplasms are frequently seen within the larynx. Most of those causing hoarseness are in close relation to the vocal cords themselves—either within the cord, projecting from its free margin, or located at the anterior commissure. Although many cases of hoarseness may be due to the presence of laryngeal tumors, malignant or benign, or to syphilis, tuberculosis and paralysis of different laryngeal muscles, it is not to be assumed that there is no such thing as simple acute or chronic catarrhal laryngitis. Cases of the former are often seen. They are usually of short duration and the result of various exciting causes. With the removal of the cause and rest of the voice, hoarseness quickly disappears in most instances. The simple chronic form of laryngitis is usually produced by long continued vocal abuse.

Psychiatric Quarterly, Albany, N. Y.

10: 531-736 (Oct.) 1936

Macroscopic Staining of the Brain: Aid in Visual Teaching of Normal and Morbid Neuro-Anatomy. F. M. Kramer, New York.—p. 533.
Autocatharsis as Therapeutic Measure: Report of Case. J. A. Brussel, Brentwood, N. Y.—p. 552.
*Cerebral Toxic Pericapillary Hemorrhage (Brain Purpura). M. Helfand and I. N. Wolfson, Poughkeepsie, N. Y.—p. 575.
Modifications of Behavior Consequent to Cerebral Lesions. K. Goldstein, New York.—p. 586.
Simultaneous Psychoses Occurring in Business Partners: Case Report. H. B. Lang, Brentwood, N. Y.—p. 611.
Technical Approaches Used in Study and Treatment of Emotional Problems in Children: Part I. The Story, a Form of Directed Phantasy. J. Louise Despert and H. W. Potter, New York.—p. 619.
Pathogenic Effect of Emotional Shock. P. Milici, Kings Park, N. Y. p. 639.
Clinical Study of Effect of Benzedrine Therapy on Self-Absorbed Patients. E. Davidoff, Syracuse, N. Y.—p. 652.
Dream Structure and Intellect. H. S. Barahal, Kings Park, N. Y.—p. 660.
Trends of Mental Disease in New York State. B. Malzberg, New York. —p. 667.

Cerebral Toxic Pericapillary Hemorrhage.—Helfand and Wolfson report a case of purpura of the brain that developed in the course of arsphenamine treatment. Statistical studies reveal its presence once in every 1,500 treated cases and its expectancy is one out of every 36,000 injections. The microscopic observations indicate that purpura of the brain may represent the end result of a series of causes entering more or less simultaneously into action. Some of the causes may be of a predisposing nature and others of a precipitating nature. In the authors' case the presence of chronic encephalitis and chronic alcoholism probably played the part of predisposing factors, which fact upholds Jakob's contention that in many cases of pericapillary hemorrhage one finds chronic syphilitic vascular changes or other preexisting vascular inadequacies. Alcohol and encephalitis may have determined the area of minor resistance. Arsenic must have played the part of a precipitating agent and may have acted both by damaging the endothelial lining elements of the small blood vessels and by producing through toxic mechanisms a damage of the perivascular tissue, thus creating one of the most essential factors in determining a hemorrhage of the brain; i. e., the presence of angiovascular and perivascular necrosis. To what extent chronic alcoholism is responsible for areas of demyelinization is difficult to answer owing to the fact that both alcoholism and arsenical intoxication may result in the production of similar areas of demyelinization. The term cerebral toxic pericapillary hemorrhage is preferred to encephalorrhagia, as it implies the suspected pathogenic mechanism of a toxic action in contrast to other forms of pericapillary hemorrhages in which hypertension and other factors may play an important part.

Public Health Reports, Washington, D. C.

51: 1429-1454 (Oct. 16) 1936

Lysine and Malignant Growth: I. Amino Acid Lysine as Factor Controlling Growth Rate of Typical Neoplasm. C. Voegtlin and J. W. Thompson.—p. 1429.
Id.: II. Effect on Malignant Growth of Gliadin Diet. C. Voegtlin and Mary E. Maver.—p. 1436.

51: 1489-1532 (Oct. 30) 1936

*Selenium Problem in Relation to Public Health: Preliminary Survey to Determine Possibility of Selenium Intoxication in Rural Population Living on Seleniferous Soil. M. I. Smith, K. W. Franke and B. B. Westfall.—p. 1496.

Selenium Problem in Relation to Public Health.—Smith and his co-workers made a survey of the rural population of parts of Wyoming, South Dakota and Nebraska to determine the possibility of selenium intoxication through the ingestion of locally produced selenium-bearing foodstuffs. A series of 111 families was studied for clinical evidence of selenium intoxication, and a series of 127 specimens of urine of as many subjects, representing ninety families, was analyzed for this element. The results of the urinary analysis showed that only 8 per cent of the cases were free or nearly free of selenium, while 92 per cent contained amounts varying from 2 to 133 micrograms of selenium per hundred cubic centimeters. This affords definite proof of the absorption of selenium by some of the rural population in the foregoing states. In the 111 families visited, the following disorders, exclusive of the more vague symptoms of anorexia, indigestion, general pallor and malnutrition, were observed: 1. Bad teeth, varying from marked discoloration through all stages of decay, were seen in one or more members of forty-eight families. 2. Yellowish discoloration of the skin, in many cases a very definite icterus, and in some cases seemingly associated with more or less definite liver disease, was seen in about forty-six subjects. 3. Skin eruptions of varying degrees of severity, but not conforming to any one particular type, were seen in twenty subjects. 4. Chronic arthritis with more or less permanent changes in the joints was present in fifteen subjects, varying from the milder types of rheumatoid arthritis to the more severely deforming type of arthritis deformans. 5. Diseased nails of the fingers, and in some cases also of the toes, were observed in eight subjects. They were usually symmetrical, atrophic, brittle and irregular and often presented transverse and at times longitudinal ridging. 6. Subcutaneous edema of probably cardiorenal origin was diagnosed in five cases, and peripheral neuritis of doubtful etiology in two subjects. Fifteen subjects gave a history of more or less protracted gastro-intestinal disturbances.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Experimental Pathology, London

17: 335-430 (Oct.) 1936

*Studies in Diphtheria Toxin Production: I. Effect of Iron and Copper. A. M. Pappenheimer Jr. and Sylvia J. Johnson.—p. 335.
Id.: II. Production of Potent Diphtheria Toxin on Simple Amino Acid Medium. A. M. Pappenheimer Jr.—p. 342.
Interpretation of Growth Fluctuations in Transplantable Tumors. F. R. Selbie.—p. 344.
Susceptibility to Tumor Growth in Rats. F. R. Selbie.—p. 348.
Studies on Neurotropic Rift Valley Fever Virus: Susceptibility of Rodents. R. D. Mackenzie, G. M. Findlay and Ruby O. Stern.—p. 352.
Immunity Reactions of Iodoproteins. I. Snapper and A. Grunbaum.—p. 361.
*Alteration in Bactericidal Power of Blood in Presence of Inflammation. W. H. Hughes.—p. 369.
Some Properties of Capsule of Pasteurella Septica. F. W. Priestley.—p. 374.
Influence of Certain Bacterial Fractions Derived from Bacteria Aertrycke on Oxygen Uptake of Rabbit Brain and Muscle Suspensions. M. E. Delafield and H. A. Smith.—p. 379.
Antibacterial Immunity to Infection with Hemolytic Streptococci in Rabbits. T. C. Stamp.—p. 391.
Centrifugation Studies: I. Critical Examination of New Method as Applied to Sedimentation of Bacteria, Bacteriophages and Proteins. W. J. Elford.—p. 399.
Id.: II. Viruses of Vaccinia, Influenza and Rous Sarcoma. W. J. Elford and C. H. Andrewes.—p. 422.

Diphtheria Toxin Production.—Pappenheimer and Johnson were led to reinvestigate the effect of inorganic salts on toxin production by the accidental observation that the yield of diphtheria toxin produced on infusion-free peptone medium increased by more than 100 per cent when Fernbach flasks made of soft glass were used instead of the usual pyrex glass. It was thought that this stimulation of toxin formation might be due to the copper or iron content of the soft glass, and these metals were accordingly studied in detail. The variation in toxin production from flask to flask, from one batch of medium to another, and the frequent inability of one laboratory to produce toxin on mediums recommended by others, may often be attributed to the variation in the concentration of iron salts in mediums and flasks. The amount of iron necessary to prevent diphtheria toxin formation is considerably less than the amount found in normal tissues. It is therefore significant that all methods for preparing toxin mediums involve the removal of a flocculent precipitate formed in alkaline solution. Excess iron is presumably removed at this point. All mediums giving a visible color test for iron with dipyridine have failed to produce any diphtheria toxin. It has often been claimed that no relationship exists between growth and toxin production; however, if the inorganic salt concentration is suitably controlled, a relationship may be found.

Bactericidal Power of Blood in Presence of Inflammation.—Hughes observed that the bactericidal power of normal blood does not fall in vitro within six hours. The blood of patients with active bacterial disease shows a steady loss of bactericidal power. Normal persons, when given vaccine, show a similar change during the stage of reaction. Blood drawn during a rigor shows one of two changes: if it is drawn at the beginning of the rigor, there is a constant low level of bactericidal power without further loss on standing; if it is drawn later, it shows a bactericidal power below normal and a progressive loss in vitro. Blood drawn after the rigor is normal. A mixture of serum taken from a patient with active bacterial disease or with an artificially produced reaction and normal blood cells shows a constant low bactericidal power with no further deterioration. The hypothesis that a toxic substance is present in the blood of patients having certain diseases, which, when it is first liberated, exerts an inhibitory effect on the bactericidal power both of normal corpuscles and of the patient's own corpuscles would appear to account for these results. The nature of the substance is at present unknown; it has been impossible to initiate the gradual loss of power by adding known substances to the drawn blood; e. g., bacterial toxin, autolyzed bacteria, filtrate of pus, or histamine. When a change followed the addition of any of these substances, it was a reduction once for all of the bactericidal power, similar to the effect of the patient's serum on normal corpuscles or of the onset of rigor. This suggests that two factors may be responsible for the gradual deterioration of certain bloods, one the toxic action of a substance liberated during the inflammatory reaction, the other an adjustment of the body to that substance. The best indication of the presence of the substance in the patient's blood was his general condition; some indication is given by the temperature, the deterioration usually being shown if this is raised.

British Medical Journal, London

2: 699-744 (Oct. 10) 1936

Spontaneous Pneumothorax. R. A. Young.—p. 699.
Substances Promoting Normal and Abnormal Growth. J. Needham.—p. 701.
Polyavitaminosis and Asulfurosis. E. J. Wright.—p. 707.
*Hodgkin's Disease and Deep X-Ray Therapy. W. L. Watt.—p. 712.
Indications for Infant Circumcision, with Notes of Simpler Operation. F. Welsh.—p. 714.

Hodgkin's Disease and High Voltage Roentgen Therapy.—Watt reviews 201 cases of Hodgkin's disease treated from 1923 to 1934. General medical treatment is extremely important throughout the whole course of the disease. Arsenic should not be given during or until six weeks after a course of irradiation. Surgical removal of glands except for emergencies appears to be of no permanent value. Ordinary x-rays act well as long as the glands are localized and superficial. Cases so treated respond afterward to high voltage irradiations just as well as untreated cases. High voltage roentgen therapy is recommended because the response to treatment is much quicker, and by varying the voltage and filtrage to suit the glands to be treated one can in a short time treat masses of glands no matter where they are situated. For superficial glands a voltage of from 160 to 170 kilovolts is sufficient, combined with aluminum filters or the equivalent of from 5 to 6 mm. thickness. A depth dose of 60 per cent of the skin erythema dose is usually enough. The spleen if palpable should receive a similar amount of radiation. The first irradiation should usually cover all the affected areas and may be spread over a period of from a week to a month if necessary. Any recrudescence should be treated at the earliest possible moment. The active focus can usually be found in persistent pyrexia. In this way, after the initial long treatment, patients are as a rule able to carry on their ordinary activities and duties with nothing but an occasional single irradiation to interfere. Periodic inspection of patients cannot be too strongly emphasized.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

43: 821-1036 (Oct.) 1936

*Mesodermal Mixed Tumors of Uterus. G. J. Meikle.—p. 821.
Diagnostic and Therapeutic Value of Uterotubal Insufflation: Study Based on 300 Consecutive Insufflations. G. King.—p. 865.
Effect of Pregnancy on Blood Pressure. J. S. Henry.—p. 908.
Mucous Colitis. J. R. Goodall.—p. 925.
Some Unusual Cases of Twin Pregnancy. Elizabeth M. Moore.—p. 936.

Mesodermal Mixed Tumors of Uterus.—Meikle reviews the literature on mixed tumors of the uterus, which are rare, and reports a new case. These tumors are composed of mixed tissues of mesodermal origin, being analogous to similar tumors found in other situations, for example the kidney and parotid gland, and only tumors including mixed tissues, as opposed to those containing mixed cells, are discussed. The mixed tissues found in these tumors are essentially heterotopic to the uterus and the tumors are highly malignant. They should not be confused with other tumors containing mixed tissues derived from a degenerative process, such as fibromyomas exhibiting fatty degeneration or calcification. Corporeal tumors are more common than those of the cervix, in contrast to the statements of other writers. There is a similarity of the age incidences in carcinoma and mixed tumor occurring in the body and in the cervix of the uterus. It is hypothesized that these tumors arise from cell rests probably activated by hormone disturbances. Of the various forms of treatment discussed, preference is given to radical surgery with postoperative roentgen therapy. The mortality is more than 90 per cent and death occurs in most cases within two years.

Gynécologie et Obstétrique, Paris

34: 257-336 (Oct.) 1936

Late Results of Ovarian Autografts with Preservation of Uterus. G. Cotte.—p. 257.
Surgical Partitioning of Douglas' Culdesac. G. Cotte.—p. 284.
Hormone Action of Acetate of Androgen on Sexual Cycle of Spleen and on Genital Tract of Doe Rabbit. G. Cotte and R. Noël.—p. 294.
Action of Dihydrofolliculin on Vegetables. C. Meyer.—p. 304.
*Premenstrual Temperature Rise in Pulmonary Tuberculosis. R. Weiller. —p. 309.

Premenstrual Elevation of Temperature in Pulmonary Tuberculosis.—Weiller states that in a large number of perfectly healthy women the menstrual periods are preceded by a slight elevation of body temperature. In patients with pulmonary tuberculosis this premenstrual rise in temperature is almost constant, and the degree to which it rises varies, depending on the individual case. In patients having healed lesions the temperature reaction is slight and analogous to that observed in healthy women. In patients with active lesions the temperature reaction is more marked, sometimes approaching a true fever. Since the degree of temperature rise is roughly parallel to the activity of the tuberculous process, the author believes that it has some prognostic significance. The explanation for this phenomenon is somewhat obscure, but several pathogenic factors enter into its causation. Menstrual detoxification, discharges of hormone and bacillemia all play an important part in the thermal instability so characteristic of pulmonary tuberculosis.

Presse Médicale, Paris

44: 1665-1680 (Oct. 24) 1936

*Treatment of Certain Articular Fractures by Procaine Hydrochloride Infiltration and Immediate Active Motion. R. Leriche and F. Froehlich.—p. 1665.
Cancer of Upper Pole of Stomach. A. Cain and P. Augier.—p. 1667.
Fold Method of Interpretation of Gastric Cavities. J. Masson.—p. 1671.
Suppurative Pleuropulmonary States. E. Piot.—p. 1675.

Treatment of Articular Fractures by Procaine Hydrochloride.—Leriche and Froehlich describe their method of treatment of articular fractures without displacement or not requiring exact reduction, by means of infiltration of the neighboring ligaments with procaine hydrochloride. By this means they hoped to block the vasomotor phenomena which tend to create a secondary arthritis and to allow active immediate motion because of the absence of pain. They obtained results which passed even their expectations. Their patients recovered with great ease in a short time and with maximal functional results. The effect of each infiltration lasts from twelve to twenty-four hours, and they repeated their injections as often as necessary. Three examples of this procedure are reported in detail. In each the results were exceptionally good. The authors believe that this method has a wide margin of application in all cases in which it is not necessary to reduce the fracture and maintain the reduction by appliances. It is curious to see how much the immediate return to function and the suppression of pain improve the quality of the results. Simple surgical common sense suffices to mark the limits of immediate mobilization after such fractures.

Helvetica Medica Acta, Basel

3: 627-736 (Oct.) 1936. Partial Index

Disturbances in Intestinal Resorption and Their Treatment. A. Gigon. —p. 627.
*Changes in Electrocardiogram After Work Test: Their Importance in Disturbances of Coronary Circulation. P. W. Duchosal and G. Henny. —p. 652.
C Hypovitaminoses. A. Jezler and H. Kapp.—p. 657.
Impairment of Liver and Porphyrin Metabolism. A. Vannotti.—p. 663.
Melanuria in Pigmentary Cirrhosis. M. Hausmann.—p. 695.
*Weil's Disease in Switzerland. O. Gsell.—p. 702.
*Significance of Determination of Diameter of Erythrocytes with Especial Consideration of Carcinoma and Ulcer of Digestive Tract. A. Alder and N. Markoff.—p. 709.

Electrocardiographic Changes After Work Test in Disturbances of Coronary Circulation.—Duchosal and Henny cite authors who made electrocardiographic studies in connection with the so-called work test in the diagnosis of disorders in the coronary circulation. To estimate the reliability of this test, they made it on ninety subjects: thirty-seven normal persons, ten patients with cardiac defects but without coronary disorders, nineteen patients with proved angina pectoris and twenty-four doubtful cases of angina pectoris. A tabular report indicates that in each of the first two groups there was one positive case. Of the nineteen patients with proved angina pectoris, eleven gave positive tests, one a doubtful one and in the remaining seven the outcome was negative. Of the twenty-four doubtful cases of angina pectoris, seven gave positive and four doubtful tests, while in the other thirteen the outcome was negative. The authors analyze these results and conclude that the work test in connection with electrocardiography has diagnostic value in the doubtful cases of angina pectoris. They think that the positive work test indicates disturbances in the blood perfusion of the myocardium but does not necessarily imply the existence of anatomic lesions in the coronary vessels.

Weil's Disease in Switzerland.—Gsell directs attention to an increase in cases of Weil's disease. Investigations in four proved and one suspected case during the summer of 1935 indicated that infestation of rivers with rats might be responsible for these cases. Some of the patients had bathed in rat-infested waters, but the author points out that working on canals or the intake of contaminated drinking water or food may likewise be a factor. He further directs attention to the fact that an increased incidence of Weil's disease has been reported also from other countries. In the completely developed cases the diagnosis is not difficult, but the abortive forms are harder to recognize. He thinks that in cases in which there are high fever, hepatorenal impairment, leukocytosis, early and great acceleration of the sedimentation speed of the erythrocytes, irritation of the bone marrow and a tendency to hemorrhagic diathesis, Weil's disease should be thought of and serologic tests should be made. The condition should be differentiated from catarrhal icterus, which usually takes its course without fever, renal involvement, increased sedimentation speed and leukocytosis. For the treatment of Weil's disease the author recommends convalescent serum, blood transfusion, infusion of fluids (to compensate for the loss of fluids), rabbit immune serum and bismuth-chiniofon.

Diameter of Erythrocytes in Carcinoma and Gastric Ulcer.—Alder and Markoff determined the mean size of the erythrocytes in 100 cases of carcinoma or ulcer of the digestive tract. In the majority of cases of gastric carcinoma they observed that a macrocytosis develops relatively early; that is, at a time when neither anemia nor anisocytosis is observable as yet. Location or duration of the carcinoma, age of the patient, existence of hepatic metastases or the state of the secretory action of the stomach has no influence on the macrocytosis. The authors think that a toxic influence on the blood formation is responsible for the development of the macrocytosis. They are convinced that a deficiency of the intrinsic factor of the antianemic principle cannot be the causal factor, because the macrocytosis is absent after gastric resection on account of ulcer but it is present in patients in whom resection has been done on account of carcinoma. They conclude that the determination of the mean diameter of the erythrocytes may in some cases be of value in the differential diagnosis of gastric carcinoma.

Giornale Veneto di Scienze Mediche, Venice

10: 645-712 (Oct.) 1936

*Ultraviolet Irradiated Blood: Therapeutic Results. B. Boggian.—p. 645.
Ether Anesthesia with Tiegel Dräger's Apparatus. T. Merler.—p. 662.
New Method of Treating Costal Fractures. Z. Bruno.—p. 666.
Hirsutism in Fetus: Case. E. Borsato.—p. 675.
Malignant Granuloma: Experimental Study of Cases. L. Pasqualigo. —p. 680.
Atypical Forms of Pneumonia with Retarded Crises in Children. F. A. Perocco.—p. 691.

Injection of Irradiated Blood.—Boggian reports satisfactory results from the administration of intramuscular injections of citrated blood subjected to ultraviolet irradiation in more than 216 patients suffering from skin diseases, acute or chronic anemia and various forms of rheumatism. The author says that the material used in the procedure should be sterilized. The layer of blood in the petri dish to be irradiated should be thin. The blood is frequently mixed by tipping the dish in the horizontal and oblique positions. For the irradiation (from

half a minute to two minutes) a modified Hanan's lamp (Bactophos) is employed. The blood is then injected in increasing doses of from 2.5 to 15 or 30 cc. for each injection. The injections are administered slowly three times a week until fifteen injections have been given. A solution of citrate can be added to the blood for maintaining its fluidity. Adding anesthetic solutions to the blood frequently results in the formation of local abscesses and diminishes the stimulating properties of the blood. The author used heterotherapy. He concludes that on ultraviolet irradiation a substance appears in the blood which stimulates the formation of erythrocytes and hemoglobin, except after splenectomy. The substance is a hormone not yet identified which exists in the blood plasma but not in blood serum. It originates in the erythrocytes, is labile to ultraviolet irradiations and paraformaldehyde and favorably modifies the consistency of the bone marrow. The failure of irradiated blood to stimulate erythropoiesis in splenectomized animals shows that the substance does not exist in the blood after splenectomy and confirms the fact that there is a relation of interdependence between the spleen and the bone marrow in the processes of erythropoiesis. The rapidity and intensity of the erythropoietic reaction of the patient to the injection depends on the amount of stimulating substance contained in the injected blood, which in turn depends on the number of erythrocytes in the donor's blood.

Minerva Medica, Turin

2: 401-420 (Oct. 27) 1936

Gastroduodenal Ulcer. L. Zoja.—p. 401.
Anatomic and Clinical Study of Extrapleural Pneumothorax. C. Rotta.—p. 404.
*Favism: Skin Reaction in Forty-Four Cases. M. Pazzi Demurtas.—p. 411.

Skin Reaction from Bean Extracts in Favism.—Pazzi Demurtas made skin reactions with extracts of beans on forty-four persons of various ages who were suffering from favism. The author states that there are three different allergens in the beans; the first is found in the flowers, the second in the seed, the coat and the shell of the beans and the third in the parasites of dry beans or in the remaining fractions of parasites in the beans. The seed allergen is the same as that of the flowers but is modified during the process of maturation of the plant, and through the modifications its biologic properties are changed. The flower allergen is more volatile than that of the seed, but the seed allergen is more concentrated. Bean allergens lose their biologic action as the beans dry up. But, as beans dry up, parasites appear within them which contain allergens with the same hypersensitizing properties as the allergens of the plant and of fresh beans. The hypersensitivity produced by the parasite does not show itself with the grave symptoms of jaundice and hemoglobinuria that are characteristic of typical favism. The symptoms are benign and sometimes there are no symptoms at all caused by parasitic hypersensitization. This is due to the biologic characteristics of the parasite. Patients who suffer a serious attack of favism are temporarily desensitized. During the period of desensitization they give negative skin reactions to the allergen that caused the attack. Desensitization in these cases is not caused by general anergy. When the patient is sensitive to various allergens the skin reaction is negative only to the allergen that caused the attack and positive to all other allergen extracts. When the patient again becomes sensitive to the allergen that caused the attack, the skin reaction becomes positive again. Some hypersensitive persons lose their hypersensitiveness after a given lapse of time. The skin reaction in these persons is never negative.

Policlinico, Rome

43: 533-592 (Nov. 1) 1936. Medical Section

Changes of Glycemia Following Insulin Injections and Simultaneous Administration of Dextrose. P. Levi.—p. 533.
*Cerebrospinal Fluid in Tetanus from Immunitary Point of View. R. Liberti.—p. 540.
Cholesterinic Lipoidosis: Case. E. Tarantelli.—p. 556.
Pathogenesis of Favism. A. Luisada.—p. 579.

Cerebrospinal Fluid in Tetanus.—Liberti states that the inoculation of large doses of cerebrospinal fluid (17 cc.) from patients suffering from tetanus failed to give tetanus to the inoculated guinea-pigs. The same negative results were obtained when the cerebrospinal fluid used in the experiment was taken after prolonged anesthesia of the patient in aseptic meningitis. The presence of antitoxin in the cerebrospinal fluid of patients suffering from tetanus who were treated by intramuscular administration of antiserum was verified. The amount of antitoxin in the cerebrospinal fluid was small compared to that in the blood, as was manifested by the antitoxic power of the blood on the one hand and of the cerebrospinal fluid on the other. The antitoxic power of cerebrospinal fluid is proportional to the intensity of meningeal irritation. It can be greatly increased by inducing meningeal irritation in the patient. According to the author, the results of the experiments prove that the toxins do not pass into the cerebrospinal fluid in tetanus and that the antitoxins pass into the fluid during antiserum treatment.

Brasil-Medico, Rio de Janeiro

50: 969-990 (Nov. 7) 1936

*Modified Staining Technic for Spirochaeta Pallida in Smears. A. G. de Castro Cerqueira.—p. 969.
Suggestion and Hypnotism. A. M. Langsner.—p. 976.
Foreign body in Respiratory Tract: Case. T. Falcão.—p. 981.

Staining Technic for Spirochaeta Pallida.—De Castro Cerqueira describes a modification of Hollande's technic for identification of Spirochaeta pallida in smears prepared from the exudates of suspected lesions. The modification consists in staining the smears with Ziehl's carbolfuchsin (instead of impregnating them by a solution of silver nitrate) and diminishing the concentration of glacial acetic acid of the original technic. Spirochaeta pallida stains smoothly and completely a clear violet pink, whereas the microscopic field stains a reddish violet. The author examined more than 2,796 smears from exudates. Spirochaeta pallida was identified in 14.51 per cent of the cases. The low percentage of positivity is due to the fact that smears were made systematically in all cases of ulcerations and excoriations of the skin and mucosa seen by the author, especially those on the genital organs, regardless of symptoms of syphilis. In several cases the positive results of the test preceded the appearance of characteristic clinical symptoms of syphilis and of chancre. The technic is simpler and more effective than other technics for identification of spirochetes, including Hollande's.

Beiträge zur klinischen Chirurgie, Berlin

164: 337-512 (Oct. 21) 1936. Partial Index

Injuries of Diaphragm. J. J. Nierstrasz.—p. 337.
*"Fish Vertebra" Disease. H. Brandt.—p. 354.
Experimental Studies on Relation of Vitamins to Infection. H.-J. Lauber.—p. 365.
Coxa Valga Luxans. A. Studemeister.—p. 370.
Recurrent Appendicitis. L. Drüner.—p. 394.
High Voltage Roentgen Therapy of Hypertrophied Prostate. K. Abel.—p. 396.
Operative Treatment of Simple Fractures. O. Kingreen.—p. 401.

"Fish Vertebra" Disease.—Brandt is inclined to consider a type of osteomalacia of the vertebral column, characterized by hour glass or "fish vertebra" deformity, an independent entity. The disease has an insidious onset with ill defined pains along the entire vertebral column, more pronounced over the lower thoracic and upper lumbar vertebrae. Examination reveals a mild kyphosis, which may be associated with a kyphotic projection of the spinous processes in the region of the tenth thoracic to the second lumbar vertebra. Blood calcium is normal or increased. Roentgenologic examination is of decisive value in the diagnosis. Stereoscopic plates taken in two planes, the anteroposterior and the lateral, reveal a lack of calcium in all the vertebrae, as well as in the bones of the pelvis and the lower extremities. The lateral view demonstrates the fish vertebra-like deformity. The pathogenesis is explained on the basis of softening of the substance of the body of the vertebra, the characteristic deformity resulting from the pressure of the intervertebral disks, which remain normal. The author proposes that this disease picture be considered an independent clinical entity to be differentiated from a purely symptomatic similar deformity caused by tumor metastases, multiple myeloma, infectious spondylitis or trauma.

SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "ME," Medical Economics; "ab," abstract; the star (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." State board examinations are entered under the general heading State Board Reports, and not under the names of the individual states. Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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Am.—American	*Med.*—Medicine
A.—Association	*Nat.*—National
Coll.—College	*Phar.*—Pharmaceutical
Conf.—Conference	*Phys.*—Physicians
Cong.—Congress	*Rev.*—Revision
Conv.—Convention	*Ry.*—Railway
Dist.—District	*S.*—Surgical
Hosp.—Hospital	*Soc.*—Society
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1— 90	1.....July 4	549— 632	8.....Aug. 22	1179—1262	15.....Oct. 10	1683—1768	21.....Nov. 21
91— 172	2.....July 11	633— 754	9.....Aug. 29	1263—1350	16.....Oct. 17	1769—1846	22.....Nov. 28
173— 246	3.....July 18	755— 836	10.....Sept. 5	1351—1424	17.....Oct. 24	1847—1934	23.....Dec. 5
247— 322	4.....July 25	837— 918	11.....Sept. 12	1425—1516	18.....Oct. 31	1935—2010	24.....Dec. 12
323— 396	5.....Aug. 1	919—1008	12.....Sept. 19	1517—1598	19.....Nov. 7	2011—2098	25.....Dec. 19
397— 470	6.....Aug. 8	1009—1088	13.....Sept. 26	1599—1682	20.....Nov. 14	2099—2222	26.....Dec. 26
471— 548	7.....Aug. 15	1089—1178	14.....Oct. 3				

An All Year Cereal Treat for Youngsters

A COLD CEREAL— IN WINTER?
CERTAINLY— WHEATIES SUPPLY AS MUCH HEAT ENERGY AS HOT CEREAL!
BESIDES, I LIKE WHEATIES, BEST!
WHEATIES

WHEATIES . . . the New Whole Wheat Cereal Creation . . . Made Especially to Appeal to Children—to Aid in Overcoming "Balky" Breakfast Appetites

NOTE: Wheaties have been accepted by the Council on Foods of the American Medical Association. This Seal of Acceptance denotes that Wheaties and advertising claims for them are acceptable to this Council.

WHEATIES have been called an "ideal cereal for children" because it has been discovered, in thousands of homes, that here is a breakfast food youngsters really "go for"—a cereal they will eat without having to be coaxed or commanded.

And Wheaties have come as a real boon to the thousands of mothers whose children do not like cooked cereal in winter. Not only are appetites tempted by Wheaties—but since they contain as many heat-producing units, per ounce of dry weight, as cooked cereal they are of equal value in helping to keep the body warm during cold weather.

Wheaties are made of whole wheat—whole wheat roasted and toasted and slightly flavored with malt until it is transformed into crispy, crunchy, golden brown flakes that are light, and gay—flakes that have the appeal, to the child imagination, of a French confection.

Wheaties are recommended the year round—a tasty, tempting breakfast treat for youngsters everywhere.

Well-known athletes in all major sports say they prefer the flavor of Wheaties. That's why this new whole wheat cereal delight, with plenty of milk or cream, sugar and some kind of fruit, has become known as a "Breakfast of Champions."

GOLD MEDAL FOODS, INCORPORATED

of Copr. 1936, by General Mills, Inc.

GENERAL MILLS, INC., MINNEAPOLIS

Breakfast of Champions

WITH PLENTY OF MILK OR CREAM, SUGAR, AND SOME KIND OF FRUIT

A shockingly large amount of dust—literally hundreds of tons—is deposited annually over each square mile of the larger urban centers. The following figures, from independent studies made over a period of years, are not isolated examples but typical of the atmospheric pollution in large cities.[1]

	Tons of dust per sq. mi. annually
Baltimore	1800
Pittsburgh	1031
Salt Lake City	349
Cleveland	780
Washington	291

In many smaller communities even worse conditions may prevail under any of the following combinations: (1) soft coal, (2) low inland wind velocity, (3) concentrated manufacturing activity, (4) no zoning regulations, (5) no smoke abatement ordinances.

It is noteworthy that even a nonindustrial city such as Washington has so high an atmospheric pollution, due mainly to smoke from residences and office buildings.

This vast amount of soot and dust cuts off light. Shrader, Coblentz, and Korff, for instance, found that the amount of ultraviolet light in Baltimore was half that 10 miles from the center of the city.[1] Under such circumstances, to rely on winter sunbaths for the treatment of rickets may prove ineffective.

a dependable antiricketic
OLEUM PERCOMORPHUM

Price Substantially Reduced Sept. 1, 1936!

At a cost to the patient of less than 1 cent a day you can prescribe 1,000 vitamin D units of Oleum Percomorphum, a dose regarded as adequate for the prophylaxis of rickets. At no additional cost the patient receives at least 7,000 units of vitamin A. Furthermore, the natural vitamins A and D in Oleum Percomorphum are in the same ratio as in cod liver oil* but in 100 times the potency. Each gram supplies not less than 60,000 vitamin A units and 8,500 vitamin D units (U.S.P.). This means that the time-tried benefits of cod liver oil without its necessarily large dose are available even to premature and young infants, who are often most in need of antiricketic therapy. Supplied in 10 and 50 c.c. bottles and 10-drop capsules (boxes of 25 and 100).

*U.S.P. Minimum Standard. [1]U.S. Public Health Bulletin No. 224.

MEAD JOHNSON & COMPANY

Evansville, Indiana, U.S.A.

Please enclose professional card when requesting samples of Mead Johnson products to cooperate in preventing their reaching unauthorized persons